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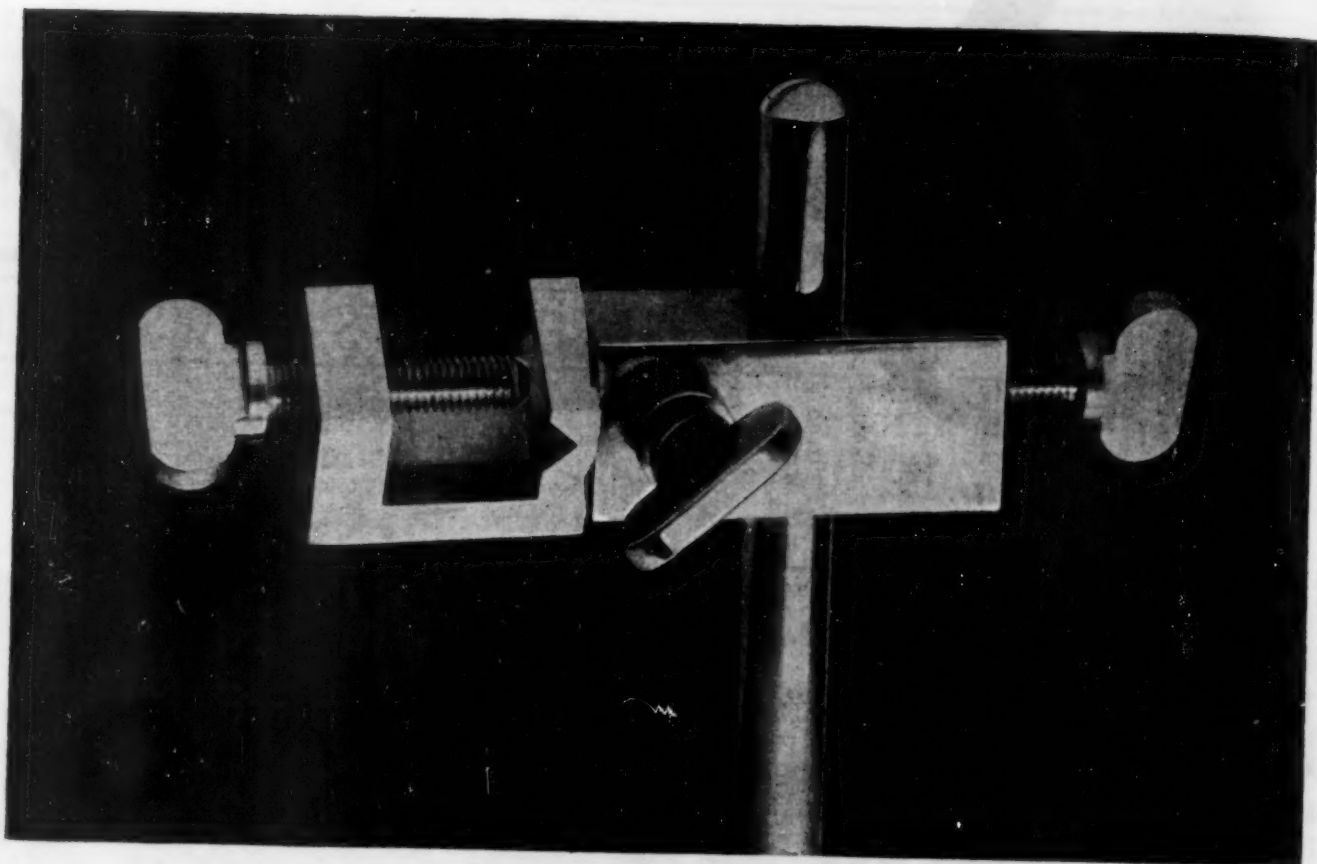
Members of the Atomic Energy Commission's Advisory Committee for Biology and Medicine, which held its first meeting in Washington, D. C., on September 12. *Left to right:* E. C. Stakman, University of Minnesota; Joseph T. Wearn, Western Reserve University; Alan Gregg, Rockefeller Foundation; A. Baird Hastings, Harvard Medical School; G. W. Beadle, California Institute of Technology; Detlev W. Bronk, Johnson Research Foundation; and Ernest W. Goodpasture, Vanderbilt University. (See *News and Notes*.)

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Discovery of Aptitude and Achievement Variables

J. P. Guilford

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# The Discovery of Aptitude and Achievement Variables

J. P. Guilford

*University of Southern California, Los Angeles*

THE PROGRESS MADE IN APTITUDE testing in the Army Air Forces during the recent war has already been discussed in *Science* (2). The brief account to follow is written with the belief that the general reader will also be interested in some of the fundamental scientific gains incidental to the AAF Psychological Program, or, more specifically, the gains in understanding the *nature* of human resources.

Under pressure of the urgent emergency during the first months of the war, the traditional approach to the development of aptitude tests for the selection and classification of pilots, bombardiers, and navigators was followed. Job analyses were made, with attempts to break the performances of men in specialized jobs into distinguishable and significant psychological functions. Tests attempting to assess those functions were constructed, and a certain degree of success was achieved. As data accumulated, however, it was recognized that the job-analysis categories were of little value in revealing why some tests were valid for the selection of good trainees, why others were not, and why some pairs of tests which appeared to be quite dissimilar exhibited substantial degrees of intercorrelation. Recourse was made to the application of factor-analysis procedures, and it soon became apparent that in this direction lay not only the answers to many puzzling questions concerning specific tests but also the general frame of reference for an enlightened test development program.

Factor theory conceives of human personality (in more operational terms, individual differences) as being economically describable by reference to a limited number of distinguishable dimensions. These fundamental variables are not readily observable by ordinary procedures because of their intricate and varied manifestations in human behavior, including that part of behavior seen under more standardized conditions, the psychological test. Tests correlate with one another to the extent that they measure in common one or more of the underlying variables or factors. From the high, low, and moderate degrees with which tests intercorrelate, the common factors can be detected by statistical operations. The attachment of psychological meaning to a factor depends upon the apparent common features of the behaviors that are symptomatic of it and upon the insight of the investigator. Several methods have been proposed for the factoring of a correlation matrix (intercorrelations among a collection of tests). Experiences of the AAF psychologists led to the adoption of

the Thurstone centroid method of extracting factors, followed by the rotation of reference axes into a positive manifold and simple structure, as being the most fruitful procedure (4). Intelligibility and reproducibility of factors and of factor loadings in tests were thus best achieved.

It is the purpose of this brief account merely to list and to define partially the factors revealed in the AAF. Verifications of previously discovered and substantiated variables, which, in tests of aptitudes, Thurstone has called "primary abilities," (5) will be mentioned first. These will be followed by a list of factors which, by their repeated verification in the AAF, can be proposed as serious contenders for recognition and by a much longer list of newcomers, the existence and identities of which require further verification.

Prewar factors verified in the AAF include:

(1) *Verbal*. This is easily verified in any test that involves individual differences in the understanding of the meanings of words. Vocabulary tests are the strongest and purest measures of it—a fact not generally accepted previously. Reading-comprehension tests have their strongest loading in this factor, but they are also usually related to others in moderate or small degree.

(2) *Numerical*. The strongest and purest tests of this factor require nothing except speed and accuracy in the four numerical operations. It tends to creep into almost any test in which numbers must be used by the examinee, not only by way of fundamental operations but also in noting number size, rank order, and the like. Its exact limits are still to be determined.

(3) *Perceptual speed*. This should more strictly be denoted as "visual-perceptual speed," for it has been observed only in visual tests. The quick, yet accurate, grasping of visual details, features, similarities, and differences seems to characterize tests heavily loaded in it. Pure tests of this factor are rather easy to achieve.

(4) *Associative memory*. Thurstone named what is probably the same factor "rote memory." This is found in tests requiring the memorizing of elements—letters, words, numbers, pictorial objects—in pairs and a later associative recall. The elements may be meaningful or nonsensical.

(5) *General reasoning*. This term is an admission of failure to identify more exactly the factor which appeared in a larger number of reasoning tests than any other reasoning factor. The test that most consistently leads in this factor is that of arithmetic reasoning. It is not a mathematical-reasoning factor, however, for it is found

in nonmathematical tests. In the AAF results there is little to support the traditional distinction between inductive and deductive reasoning abilities. No reasoning test was pure in any factor. Since all tended to be factorially complex, definitions of the three reasoning factors could not be achieved. One hypothesis is that the general-reasoning factor represents a diagnostic ability—the ability to grasp the nature of problems.

The next factors are fairly well verified. Only one (visual memory) has a clear prewar counterpart.

(6) *Spatial relations*. One of the most significant AAF findings was the separation of this factor and the next one, called *visualization*. It seems quite clear that prewar results had confused the two. Thurstone called his primary ability in this area “space,” but he defined it as if it were visualization (5). The space factor, as here defined, is found in psychomotor tests as well as in printed tests. It seems to be a perceptual awareness of the arrangements of objects with respect to right-left, up-down, and out-in dimensions. Correct choice as to direction of movement in some psychomotor tests depends upon it.

(7) *Visualization*. This factor, which should probably be modified to “manipulatory visualization,” is prominent in tests requiring one to imagine transformations, movements, or other changes. A typical test presents a picture of a square paper being folded one or more times, in successive steps, and a hole of a given shape being cut out. The examinee selects one of five other pictures, each showing plausible creases and holes, as the paper might appear after being unfolded.

(8) *Mechanical experience*. The AAF analyzed almost every type of so-called mechanical tests. Printed tests often designated as “mechanical” showed, depending upon the test, moderate loadings in perceptual speed, spatial relations, and visualization. Many of them showed loadings in a factor which compelled the conclusion that its existence depends heavily upon learning—hence the factor name, “mechanical experience.” Tests of mechanical information (stressing knowledge of tools and automobile parts and their functions) are almost unique in this factor. The popular term “mechanical aptitude” covers a rather loose collection of things and, when used, should be carefully scrutinized. Mechanical jobs vary all the way from tinkering with clocks and operating a steam shovel to designing a bridge. Each job, though called “mechanical,” probably has its unique pattern of requirements in terms of human resources.

(9) *Length estimation*. Probably the best test of this factor is one requiring a simple and direct comparison of the lengths of lines. The factor also appears in tests involving objects of more than one dimension. Its degree of generality has not been determined.

(10) *Visual memory*. This factor, which seems to be a purely reproductive type of memory for visual patterns,

can probably be identified with a similar factor found by Carlson before the war (1). It is found in recognition tests as well as recall tests and might be regarded as a second and independent type of visualization. Both this and the manipulatory-visualization factor would be expected to depend upon the visual cortex, and in view of their independence, one should look for two distinct corresponding properties of that cortex. In this connection, one is reminded of the distinction made in two types of eidetic imagery—rigid and plastic.

(11) *Judgment*. Job analysis, of the pilot's work in particular, stressed the paramount importance of what is popularly known as “common-sense judgment.” Tests called “practical judgment” were therefore constructed. These presented items in the form of verbally described predicaments such as those a service man might encounter, each with five more or less plausible solutions, one of which was regarded as the wisest under the circumstances. Analysis of such tests showed significant loadings in the verbal factor, in general reasoning, and in the mechanical-experience factor. (Knowledge of common tools and materiel was apparently useful to the examinee in this kind of test.) Over and above these variables common to the practical-judgment tests, there was additional communality which could be called judgment. While it was characteristic of judgment tests as a class, it was also common to tests calling for practical estimations of sizes, times, and distances in everyday situations and to some tests of planning. It may actually be a fourth kind of reasoning—that is, reasoning of a judicial or critical type. It is probably a factor that is almost entirely missed in most intelligence tests, which supports many a layman's view that common-sense judgment is not covered by the IQ.

(12) *Psychomotor coordination*. This factor is common to various psychomotor tests, including those requiring coordinations of fingers and hands (finger dexterity), of arm and shoulder (rotary pursuit), and of arms and legs (using mock airplane controls). It is doubtful whether it can be identified with the agility factor found in such physical education tests as the dodge run. It is quite possible that there is a coordination factor other than this one which is restricted to the finer finger movements.

The remaining factors are merely suggestive of worth-while hypotheses.

(13) *Psychomotor precision*. This was found to be common to a finger dexterity test, a discrimination-reaction time test that required rather accurate aiming at the reaction keys, and the pass-fail criterion in bombardier training. It is hoped that the naming is more than a figure of speech in its association with precision bombing!

(14) *Psychomotor speed*. This appeared in only two rather unique paper-and-pencil tests in which the rate of marking an answer sheet was important. It strongly



suggests a prewar factor in similar tests, such as the speed of making "gates" (tally marks). Little more can be said of it at this time. Hypothetically, it would be important in the more simple, repetitive tasks of motor performance.

(15-16) *Reasoning II and reasoning III*. These two factors arose rather weakly in a number of factorially complex tests. Clues for hypotheses are seriously lacking. Reasoning II is prominent in analogies tests and the hypothesis of "reasoning-by-analogy" is tempting, but it also appears in other tests not obviously having this quality. Reasoning III is strongest in two tests, one of which seems to call for inductions (seeing systems in arrangements of lines) and one for deductions (deciphering a code). The finding of at least three distinct reasoning factors suggests that the term "reasoning" conceals a number of unrecognized functions. Some of these may be primarily biologically determined, but others may be in the form of reasoning habits brought about under educational pressures, formal or otherwise. Until the variables are better identified in this area, studies of training in thinking and of the problems of formal discipline cannot be adequately effected.

(17-18) *Space II and space III*. These factor names are not only very general but also highly tentative. Space II is prominent in two of Thurstone's space tests involving the ability to recognize from pictures of human hands held in varied positions whether each picture is of a left or a right hand, in the one, and the ability to tell whether two U. S. flags, as pictured, show the same or the opposite sides, in the other. One hypothesis is that kinesthetic imagery plays a role in the solution of such items for some individuals. There is no suitable hypothesis to offer for space III.

(19-20) *Memory III and memory IV*. A third memory factor was strongly common to two tests. The task was one of paired associates in which names were memorized for objects: airplanes in one test and outline lakes, rivers, and bays in the other. These tests also had in common the more general associative-memory factor previously mentioned. This fact, taken together with that of several reasoning factors, suggests the possibility of hierarchies of factors within an area of mental functioning, with different levels or different degrees of generality, or both. It would seem that, although such functions are statistically independent or at least separable, they quite commonly operate conjointly in behavior. Memory IV is named as such with considerable hesitation. It could be defined as memory for verbal instructions or, generalizing somewhat, as memory for verbal content. This factor was found in a small number of tests having in common intricacy of instructions and tasks. Forgetting any part of the directions while attempting an item might well result in failure on the item. The tests were designed to see how well the prospective pilot could "keep in mind" a number of things

that had to be taken into consideration in performing a task. One memory test (called Memory for Tactical Plans), which consisted of a quizzing two hours later on a briefing given orally for a mock military mission, although not analyzed along with the tests just mentioned, was known to have an unknown factor or factors related to the criterion of pass-fail in pilot training over and above factors already accounted for. It is a reasonable hypothesis that "memory for instructions" is common to this test and those known to be loaded in memory IV.

(21-22) *Mental set I and mental set II*. The first is strongest in tests of following directions when these keep changing as the examinee proceeds. There is little for the examinee to remember for very long. The significant variable seems to be an adaptability to changing rules. It is not a matter of flexibility of set, in a sense opposite to perseveration. Explicit attempts to bring out an expected common factor of perseveration in a number of tests definitely failed. Mental set II seems to represent a breadth-of-set quality. Attention to details, overlooking none, seems relatively important. The tests in this cluster are tedious, exacting tasks. Whether definition of the factor should emphasize breadth or care in handling details is an open question.

(23) *Carefulness*. This and the next factor seem to be temperamental or motivational variables rather than abilities. It was hypothesized that navigators must exercise extreme care with details in their work, for small mistakes become magnified in terms of miles-off-course and errors in estimated time of arrival. Four tests of a complex, clerical type were devised to study this hypothesis. Analysis of the scores based upon the number of items correct yielded some of the already familiar factors in significant amounts—number, visualization, and space. The scores based upon the number of errors made, however, had in common a new factor which could very reasonably be called carefulness. Its possible relations to mental set II have not been investigated. This might be denoted as "meticulousness," a personality trait that has already been given some attention by clinical psychologists. Of great general importance in this finding is the fact that error scores and correct responses may measure something very different. It has generally been assumed that "rights" and "wrongs" in a test measure the same functions in reverse direction. The finding opens the door to a promising line of new research.

(24) *Pilot interest*. From the finding of this unity in behavior, one is led to the conclusion that our culture has molded an interest variable centering around piloting an airplane. It seems not to be a general aviation interest, and no similarly crystallized interest variables for navigation or for bombardiering were noted. The pilot-interest factor was revealed in general-information tests (which included items on knowledge

of airplanes and their operation) and in a biographical-data test score that was valid for pilot selection. This test called for facts concerning the examinee's previous flying experience, hobbies, and the like.

(25) *Mathematical background.* This is common to the biographical-data test as scored for the selection of navigators and to mathematics-achievement tests (including algebra, with some trigonometry and analytical geometry). It has no relation to numerical-operation tests or to arithmetical-reasoning tests. Like the mechanical-experience factor, it seems to be a culturally determined unity in individual differences.

(26) *Social-science background.* This is mentioned with extreme hesitation because it was revealed in conjunction with only two tests—information tests in history and geography. The only other supporting evidence, (and it is quite slender) is that this factor correlates slightly negatively with the pilot criterion, which is also true of biographical indications of specialization in the social sciences. This hypothesis suggests the question of whether there is also a physical-science background factor. Since only one field of physical science—physics—was examined in aviation students, this hypothesis could not be tested.

(27) *Planning.* The name of this factor is adapted from the planning tests, in which it is unique. One test of this kind required the examinee to tell in which order he would make the strokes of two successive letters if he were skywriting with an airplane. Another called for the most economical order for a series of errands to be performed in a city whose layout is pictured. This factor might possibly be another kind of visualization, but, unlike the manipulatory visualization, it calls for more of a creative contribution. It is distinct from the judgment factor, although both may occur in the same tests.

As a general consideration, there is always the question of whether factors are completely independent or correlated to some degree. Almost exclusively, orthogonal frames of reference were used in the AAF for describing factor configurations. There seemed to be no evidence of very significant correlations among the factors. The matter has recently been given some attention. There are probably some small correlations among some of the intellectual and perceptual factors. An interesting, slight, negative correlation appeared between the number factor and the mechanical-experience factor. The probable reasons for this are not hard to surmise.

The list of factors is probably longer than many would expect, and yet it is certainly not exhaustive. The fact that other previously reported factors did not

emerge should not be taken as evidence against their existence. The absence of a universal or "g" factor in Spearman's sense, however, is a significant outcome.

The list throws into bold relief the limitations of intelligence tests and the IQ. These ordinarily stress most heavily the verbal, general-reasoning, and numerical factors, probably in that order, with sprinklings of contributions of space, visualization, and memory depending upon the test. The IQ, as derived from different tests, is not a constant article by any means. IQ tests would have been almost useless in selecting pilots from among those with IQ's of 100 and above had mastery of flying training been the criterion. On the other hand, it was estimated that the pilot criterion leaned most heavily upon such resources as spatial relations, mechanical experience, psychomotor coordination, pilot interest, and perceptual speed, with minor dependence upon about 15 of the other factors in the list. Even then, with all these factors optimally weighted in a composite aptitude score, less than 60 per cent of the variance in the pilot criterion would be accounted for. Within the limitations of the reliability of the criterion itself, perhaps as much as 80 per cent could be predicted if all pertinent factors were included in the aptitude composite (3). Before the war, a selective test or battery would have been regarded as relatively successful if it accounted for as much as 30 per cent of the variance in a practical criterion.

The vocational implications of all this are quite clear. Fitting individuals to educational and vocational plans presents a much more complicated problem than has heretofore been supposed. The chief hope for a solution appears to lie in the direction of the use of factorial thinking and practice. Persons, tests, and jobs can all be described in terms of the same reference frame—one with which many can agree because it is derived in an operational manner. Not only aptitudes, whether biologically or culturally conditioned, or both, but also temperamental and other personality traits can be translated into the same types of categories. It is probable that substantial gains in the assessment of all aspects of personality await such an approach. It is also probable that controlled fundamental research on other problems of human nature awaits the identification of its real variables.

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## Educational Programs at Research Centers

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THE ACUTE SHORTAGE OF COMPETENT scientific personnel, which endangers the research and development programs of the Nation, has been the subject of considerable discussion. An interesting summary of several factors affecting research and some noteworthy suggestions for measures to improve conditions were presented by Charles V. Kidd in the January 14 issue of *Science*. However, this article failed to mention the steps that can be taken at industrial or government research centers to improve the competence of personnel through educational programs within the centers.

In a later issue (May 2), Kenneth A. Meade stated the case of the industrial concern very comprehensively and in considerable detail. In general, his conclusions and comments are very appropriate. For example, the staff at this Laboratory heartily agrees that the essential training to be given by educational institutions should consist of a good grounding in the fundamentals. One point of possible disagreement is Meade's conception that the educational institution can help a young man finally determine whether his interests lie in engineering, teaching, or sales work. Actual work on a job is frequently required to make this determination.

The experience of the Navy Electronics Laboratory in inaugurating and carrying out a program of in-service education may be of interest to others. This program appears to have helped not only in overcoming some of the deficiencies in the backgrounds of available personnel but also in aiding those who are uncertain as to their fields of work to decide on a course of action. Although somewhat simpler of accomplishment in a government research and development center, it is believed that the program, which is based on the good democratic principle that "the Lord helps those who help themselves," is not inapplicable to industrial groups.

A survey showed requirements at four levels. First, there was a need for interchange of scientific knowledge and ideas between more experienced and less experienced scientists at the Laboratory on a general, rather than a work assignment, basis. Second was the requirement for upper-division, college-level courses to afford opportunity to promising younger men to finish undergraduate instruction. There was also the need of older men to extend their knowledge into new fields. Third, men working for higher degrees required assurance of opportunity. Fourth, and most important, was the necessity of tapping the knowledge of eminent scientists in special fields.

The whole in-service educational program is loosely integrated by the Educational Board of senior scientists,

which is also responsible for direct action on the more formal portions of the program. The Educational Board also attempts to cover one or two other points raised by Meade. For example, it can advise and all but direct younger men to undertake certain courses of instruction, and it can also discourage those who are ill fitted for other courses in the interest of keeping classes at convenient working size.

The exchange of information and ideas between staff members takes place in two fashions. Several departments operate seminar series, on the basis of mutual contribution of effort. The visits of outside scientists and senior staff members are also seized as opportunities for scientific "bull sessions" with all members of a group contributing.

Regular courses are given that range from straight undergraduate work to graduate-level seminars.

Generally speaking, undergraduate classes are handled by the University of California's Extension Division. Some of the upper-division and graduate courses are given by staff members and some by visiting consultants. These courses and teachers are cleared with the University of California at Los Angeles. By this method, and through arrangements with the Graduate School of the University, staff members acceptable to the Graduate School may obtain graduate credit for such accredited courses taken at the Laboratory. This encouragement of further graduate work has been strongly and enthusiastically supported by the younger men and women of the Laboratory.

It has been found impracticable to establish fixed rules for time scheduling of courses. Instead, each one is considered on its merits, depending upon the direct applicability to Laboratory work, benefits to individuals, and other factors. As a result, some instruction is given during working hours, some out of working hours, and some overlaps at the end of the day.

The most interesting and unique part of the program is that filled by the visiting consultant. Leading scientists of known and outstanding ability in fields related to, or directly in line with, the work of the Laboratory are brought in for limited periods to act as consultants and instructors.

In the role of consultant, the visiting scientist contributes both directly and indirectly to the work of the Laboratory. In some cases he may assume a definite problem in research or development during his residence, planning an investigation and supervising the work of staff scientists. If the project is small, he may complete the investigation during his stay. If the problem involves

long-term research, he will plan and organize a program which will be carried on by Laboratory men. The visitor is, therefore, directly responsible for a portion of the research program. He also makes direct contributions, sometimes accidentally, to other related investigations. For example, the informal discussion by a visiting scientist of a new method of mathematical analysis saved two months of work for the Laboratory. The technique, hitherto unknown, was applied to a problem and the solution obtained immediately. The long analysis program previously planned was cancelled.

Instruction may be handled in several ways. The visiting scientist may present a series of lectures covering some specialized field, ordinarily at college upper-division or graduate level. He may, in addition, present even more specialized material, usually the result of his own research, to a smaller group in seminar-type meetings.

The benefits to the Laboratory are obvious, and the program is effective in several ways. The younger staff members have an opportunity not only to increase their knowledge in the basic principles and methods necessary to the conduct of their work but also to learn new techniques and developments. Those scientists directing the research and development program of the Laboratory can learn firsthand the status of research being conducted by other organizations in allied fields. The wider the knowledge and the greater the ability of the staff scientists, the sooner will the research problems be solved. These benefits are not always measurable, but examples of concrete results are frequent. In one case, a research problem assigned by the Bureau of Ships was solved by applying certain newly discovered principles to previously collected data, and a tedious experimental period was avoided. The solution, later checked by a brief series of experiments, proved correct. This was possible only because a visiting scientist had explained the new principles in a series of lectures given several months before assignment of the problem. The Laboratory scientist, by referring to his notes, was able to apply the new information to his data, thus effecting a considerable saving in time and money.

The indirect influence of the visiting scientist, though generally intangible and difficult to identify, is perhaps his most valuable contribution. The spontaneous interchange of ideas among scientists is the best stimulus for scientific progress. The effect on Laboratory personnel of the different outlook, attitude, and ideas, as well as the wide knowledge, of the visiting scientist can only be described as inspirational. Its value to the Laboratory lies in the increased potential ability of the staff scientist rather than in the solution of specific problems.

Many of the results of this program are, of course, of benefit to the visitors as well as to the Navy Electronics Laboratory. The visitors have an opportunity to review much of the Laboratory's program, to discuss their own research problems with staff scientists, and to use the extensive Laboratory facilities for experimental work.

This advanced educational program began in the summer of 1946. The Navy Electronics Laboratory was fortunate that the first scientists to visit the Laboratory as consultant-instructors were R. B. Lindsay, chairman of the Physics Department, Brown University, and S. A. Schelkunoff, of the Bell Telephone Laboratories. Prof. Lindsay lectured on wave motion with particular application to acoustics and radio, while Dr. Schelkunoff gave a series of lectures on special topics in applied mathematics of considerable importance in wave propagation and radiation from antennas. After several conferences and symposia, both scientists were able to make many suggestions of value to present and future investigations.

W. G. Cady, of Wesleyan University, visited the Laboratory from the latter part of February to April of this year, presenting one series of lectures on "Piezo-electric Theory" and another on "Transducer Design." During the summer, Henry Margenau, of the Physics Department, Yale University, presented a course on "The Mathematics of Physics and Engineering" and also offered a seminar on "Transmission of Microwaves Through Gaseous Media." The subject matter covered by these men, both authorities in their fields, has direct and immediate application to the work of the Laboratory.

Every effort is being made to schedule visits of others in a similar capacity during future sabbatical leaves or summer vacations. Present plans include a course on "The Kinetic Theory of Gases" by Leonard B. Loeb, Department of Physics, University of California, Berkeley.

In the future, it is planned to improve continually the available educational opportunities at the Navy Electronics Laboratory. There is no reason why, eventually, the point cannot be reached at which a stimulating atmosphere of learning and free discussion exists throughout the Laboratory to the same degree as at academic institutions, where much smaller scientific groups working in close collaboration make such an ideal situation more easily attainable.

Meade has, further, raised the point that technical schools must be furnished with pertinent information on the policies, management philosophies, and attitudes expected of graduates employed by various institutions. The Navy Electronics Laboratory has recently published a brochure, covering these fundamental points and many others, which has been given wide distribution to educational institutions. It is hoped that, in addition to its uses in recruiting personnel, this information will be helpful to these institutions.

It is the firm conviction of the staff that all of this effort is worth while. The scientific stature of individuals at the Laboratory will be increased, and the whole program of the Laboratory will benefit. In addition, some small contribution to the scientific manpower resources of the country will be made through the encouragement of the younger men.



# NEWS

## and Notes

Seven of the Nation's leading scientists have recently been appointed by the U. S. Atomic Energy Commission to membership on an Advisory Committee for Biology and Medicine. Chairman of the group is Alan Gregg, director for medical sciences, Rockefeller Foundation, who will be assisted by G. W. Beadle, chairman, Division of Biology, California Institute of Technology; Detlev W. Bronk, director, Johnson Research Foundation, and chairman, NRC; Ernest W. Goodpasture, dean, School of Medicine, Vanderbilt University; A. Baird Hastings, professor of biochemistry, Harvard Medical School; E. C. Stakman, chief, Division of Plant Pathology and Botany, University of Minnesota; and Joseph T. Wearn, dean, School of Medicine, Western Reserve University.

Among the tasks confronting the Committee are the nomination of a director of the Commission's proposed Division of Biology and Medicine; a study of basic policies which the Commission should follow with respect to the biological, medical, and health physics aspects of its program; a study of possible ways of utilizing an appropriation of \$5,000,000 for cancer research; and formulation of plans for carrying out the long-range recommendations made to the Commission by the Medical Board of Review. The latter include such problems as extension of research and training in the application of atomic energy to medical and biological problems; health hazards; continued provision of isotopes for research purposes as well as provision of a consulting service for investigators; publication of scientific papers; cooperation between the Commission and other agencies of the Government

with respect to fundamental research and the training of personnel; and provision of fellowships in the field of radiation effects.

A partial list of headquarters assignments for the sections and societies that will meet with the AAAS at Chicago, December 26-31, 1947, is given below. The Sherman Hotel will be the general headquarters for the convention.

**Congress Hotel:** American Association of Economic Entomologists, American Microscopical Society, American Society of Naturalists, American Society of Parasitologists, Beta Beta Beta, Ecological Society of America, Entomological Society of America, Phi Sigma Society (Council only), Society for the Study of Evolution.

**Palmer House:** Section B (Physics), Section O (Agriculture), American Association of Physics Teachers, American Dietetic Association, American Meteorological Society, American Physical Society, American Society for Horticultural Science, Honor Society of Phi Kappa Phi, Philosophy of Science Association, Pi Lambda Theta, Potato Association of America, Sigma Pi Sigma, Society for Research in Child Development.

**Sherman Hotel:** Section A (Mathematics), Section C (Chemistry), Section D (Astronomy), Section E (Geology and Geography), Section H (Anthropology), Section I (Psychology), Section K (Social and Economic Sciences), Section L (History and Philosophy of Science), Section M (Engineering), Subsection Nd (Dentistry), Subsection Nm (Medicine), Subsection Np (Pharmacy), Section Q (Education), Academy of World Economics, American Chemical Society (Chicago Section), American Nature Study Society, Cooperative Committee on Science Teaching of AAAS, National Association of Biology Teachers, National Science Teachers Association, Pi Gamma Mu, Research Council on Problems of Alcohol, Sigma Delta Epsilon, Society of the Sigma Xi.

**Stevens Hotel:** Section F (Zoology), Section G (Botany), American Fern Society, American Phytopathological Society, American Society of Plant Physiologists, American Society of Plant Taxonomists, American Society of Zoologists, Botanical Society of America, Inc., Genetics Society of America, Herpetologists

League, Limnological Society of America, Mycological Society of America, Sullivant Moss Society.

**Receipt of back issues** of *Science* for the entire year 1947 from members of the AAAS who do not maintain permanent files would be greatly appreciated (see *Science*, May 16). Those especially needed at the moment, however, are Nos. 2717 through 2726, 2728, 2730, 2731, 2733, 2734, and 2740 through 2742. The issues should be sent by second-class mail to: American Association for the Advancement of Science, 1515 Massachusetts Avenue, N. W., Washington 5, D. C. Postage will be refunded.

### About People

**Marian Balicki**, of the Polish University College, London, has been appointed assistant professor of mechanical engineering at the Polytechnic Institute of Brooklyn. Dr. Balicki last spring was awarded the Andrew Carnegie Silver Medal for research on work hardening and recrystallization of Armco iron.

**Angel Cabrera**, professor of zoology, University of Buenos Aires, and **Rudolph M. Anderson**, curator of Mammals, emeritus, National Museum of Canada, were elected to honorary membership in the American Society of Mammalogists at the 27th annual meeting of that organization.

**Harvey S. Moyer**, professor of chemistry, Ohio State University, has been appointed an assistant dean of the Graduate School. Dr. Moyer will devote half time to his new duties.

**Lt. Col. George W. Hunter, III**, formerly chief, Department of Parasitology, Army Medical Department's Research and Graduate School, Washington, D. C., is now serving a tour of duty overseas, having been assigned as chief of the Section of Medical Zoology, 406th Medical General Laboratory, located in Tokyo, Honshu, Japan.

**Eugene L. Lopez**, a member of the University of Illinois staff since 1937, has been appointed director of clinics at the University of Illinois Hospitals.

**Herman V. Tartar** has been appointed executive officer of the Department of Chemistry and Chemical Engineering, University of Washington,

Seattle. A member of the staff for 29 years, for the past 5 years he has served as director of the laboratories.

**William A. Perlzweig**, professor of biochemistry, Duke University School of Medicine, has received three months leave to visit Palestine, where he will act as special adviser to the Hebrew University and the Hadassah Medical Organization in the proposed establishment of a medical school in the University of Jerusalem.

**David F. Miller**, professor of zoology, Ohio State University, has been named chairman, Department of Zoology and Entomology, which embraces zoology, entomology, genetics, and conservation. Dr. Miller succeeds **Laurence H. Snyder**, recently named dean of the Graduate School, University of Oklahoma.

**A. Starker Leopold**, **Frank A. Pitelka**, and **Ralph I. Smith** have been promoted to assistant professorships in zoology at the University of California, Berkeley.

**Irvine McQuarrie**, head, Department of Pediatrics, Medical School, University of Minnesota, has been commissioned by the Rockefeller Foundation to make a three-month survey of the status of medical education and the standards of medical practice in postwar Japan. He left for the Orient by plane September 16.

**George B. Barbour**, dean, College of Liberal Arts, and professor of geology, University of Cincinnati, has recently shown that caves at Makapan, near Johannesburg, South Africa, are similar in formation and deposits to those once inhabited by China's prehistoric Pekin Man. As a result of Dr. Barbour's investigations, the University of California is preparing to send an expedition which will open its research at Sterkfontein where the Transvaal Sterkfontein Man was discovered by Robert Broom. The expedition hopes to recover in the Makapan Caves the remains of men living there more than 250,000 years ago. Stone implements, animal bones, and a stone hearth have already been uncovered there.

**Lloyd M. Bertholf**, since 1924 professor of biology and since 1939 dean of the faculty at Western Maryland College, Westminster, Maryland, has accepted the deanship of the College of the Pacific, Stockton, California, effective February 1, 1948.

**Col. Marshall Stubbs** has been appointed deputy chief, and **Maj. Claude W. White** executive officer, of the Research and Engineering Division, Army Chemical Center, Maryland, according to an announcement by Col. Charles E. Loucks, chief of the Division. This Division directs and coordinates the research and development program of the Chemical Corps. In addition to work on chemical agents, the research program includes the development of smoke, incendiary, weapons and munitions, protective devices, and all countermeasures in these fields.

**David L. Taylor**, Department of Botany, University of Chicago, has been appointed assistant professor of botany at the University of Illinois.

**Erich Lindemann**, psychiatrist, Harvard Medical School, has been appointed to the Harvard University Faculty of Arts and Sciences to assist in broadening the scope of the new Department of Social Relations, established last year to break down the limitations of individual departments in working on common problems of social relations. Dr. Lindemann will continue as a member of the staff of Massachusetts General Hospital.

**Percival Bailey**, neurologist, University of Illinois, has been promoted to distinguished professor of neurology and neurological surgery, becoming the second faculty member of the Chicago Professional Colleges to hold the distinguished professor rank.

During the summer session at **Northwestern University**, completed August 23, **William N. Fenton**, senior ethnologist, Bureau of American Ethnology, Smithsonian Institution, lectured on primitive political organization, and **C. F. Voegelin**, professor of anthropology and chairman of the Department at Indiana University, taught linguistics. Both visiting professors taught general anthropology. Dr. Fenton resumed his regular work at the Bureau of American Ethnology on September 15, after a brief field trip among the Seneca Indians of western New York; he is currently senior editor of the *Journal of the Washington Academy of Sciences*. Dr. Voegelin, who has returned to Bloomington, edits the *International Journal of American Linguistics*.

**Harry L. Fevold**, head, Pharmaceutical Food Proteins and Food Lipids Sec-

tion, Biochemical Division, Western Regional Laboratory, U. S. Department of Agriculture, Albany, California, has been appointed chief, Product Development Division, Quartermaster Food and Container Institute for the Armed Forces, Chicago.

**Samuel R. Tipton**, associate professor of physiology, Medical College of Alabama, has been appointed professor of zoology, University of Tennessee.

**Edward B. Tuohy**, formerly associate professor of anesthesiology, Mayo Clinic, has been appointed professor of anesthesiology, Georgetown Medical Center, Washington, D. C.

**Ray T. Wendland**, assistant professor of chemistry, Lehigh University, has been appointed professor of chemistry, Organic Section, North Dakota State College.

## Grants and Awards

**Arpad L. Nadai**, consulting engineer of the Westinghouse Research Laboratories, has been awarded the Worcester Reed Warner Medal by the American Society of Mechanical Engineers. The medal, which is given for noteworthy contributions to the permanent literature of engineering, will be presented at the Society's annual meeting in Atlantic City in December.

**Van R. Potter**, McArdle Memorial Laboratory for Cancer Research, University of Wisconsin, received the \$1,000 Paul-Lewis Laboratories Award in Enzyme Chemistry at the recent meeting of the American Chemical Society for his contributions in the field of respiratory enzymes.

**Nominations are solicited for the 1948 Award of \$1,000** established by Mead Johnson and Company to promote researches dealing with the B-complex vitamins. The recipient of this award will be chosen by a Committee of Judges of the American Institute of Nutrition, and the formal presentation will be made at the annual meeting of the Institute in the spring of 1948.

The award will be given to the laboratory (nonclinical) or clinical research worker in the United States or Canada who, in the opinion of the judges, has published during the previous calendar year the most meritorious scientific report dealing with the field of the B-



complex vitamins. While the award will be made primarily for publication of specific papers, if circumstances and justice so dictate, it may be recommended that the award be made to a worker for valuable contributions over an extended period, but not necessarily representative of a given year. Membership in the American Institute of Nutrition is not a requisite of eligibility. Nominations for this award for work published in 1947 must be in the hands of the Nominating Committee by January 10, 1948, and should be accompanied by such data relative to the nominee and his research as will facilitate the task of the Committee of Judges. E. N. Todhunter, University of Alabama, University, Alabama, is chairman of the Nominating Committee.

At the opening sessions of the World Conference of the International Federation of University Women, August 12, in Toronto, the following recipients of awards were named: The international fellowship in senior science (\$300) went to E. J. Batham, Otago University, New Zealand, to continue research in zoology at the University of Cambridge; the Helen Marr Kirby Fellowship, to G. F. E. M. Dierick, University of Amsterdam, who will continue studies in the chemical control of citrus pests in California; the International Fellowship, to Mrs. H. Zwirn-Hirsch, Hebrew University, Jerusalem, who will continue research in fungi in California; and an award to L. C. Roubert, chemist, Algiers University, who will work on blood proteins at Harvard Medical School.

The American Cancer Society has made a grant of \$10,000 for the support of special research on the growth of cancer cells to the Tissue Culture Laboratory, University of Texas Medical Branch, Galveston, which is under the direction of Charles M. Pomerat.

Claude E. Zobell, professor of microbiology, Scripps Institution of Oceanography, has been awarded a special fellowship by the Rockefeller Foundation which provides for a year of travel and study in European research laboratories.

## Colleges and Universities

A new course in the colloid chemistry of silicon is being established this fall at Massachusetts Institute of Technology. This course, which will be

under the direction of Ernst A. Hauser, associate professor of chemical engineering, will be a survey of the chemical and physical properties of substances containing silicon as their basic constituent in correlation with their molecular structure.

Studies of human heredity being conducted at the University of Michigan under the sponsorship of Lee R. Dice and for the past 7 years supported by annual grants from the Board of Governors of the Horace H. Rackham School of Graduate Studies, will henceforth derive about half of the necessary support from the Laboratory of Vertebrate Biology. The remainder of the support for the work continues for the current year to be provided by a grant from the School of Graduate Studies. Among those engaged in the project are C. W. Cotterman (full time); Harold F. Falls, Department of Ophthalmology, who is cooperating actively; Sidney L. Halperin, Neuropsychiatric Institute, who is initiating studies of the heredity of mental deficiency; and Avery R. Test, Mary Jane Lagler, and Byron O. Hughes. James V. Neel is temporarily on leave for Army service.

The Polytechnic Institute of Brooklyn will offer the degree of Doctor of Philosophy in Applied Mechanics, beginning with the current semester. Thesis subjects for the new degree will be in the fields of theory of elasticity, theory of plasticity, theory of structures, aerodynamics, hydrodynamics, gas dynamics, or the theory of vibrations. Last year the Institute introduced a new curriculum leading to the degree of Master of Science in Applied Mechanics to make available to graduate engineers a broad knowledge of the principles of mechanics which became so important in the new concepts of design developed during the war. These studies were incorporated in the expanded Department of Aeronautical Engineering under the title of the Department of Aeronautical Engineering and Applied Mechanics, headed by R. P. Harrington.

Glenn T. Seaborg, director of chemistry, Radiation Laboratories, University of California, Berkeley, and Sir Ian Morris Heilbron, director, Chemical Laboratories, University of London, England, will deliver special lectures at the University of Notre Dame during the current academic year. During the week of November 17 Dr. Seaborg will deliver

the 1947 Nieuwland Memorial Lectures in Chemistry, a series established by Notre Dame to honor the memory of the late Rev. Julius A. Nieuwland, C.S.C., who conducted research at the University leading to the discovery of the basic formula for synthetic rubber. Sir Ian will be the first Reilly Lecturer in Chemistry and will visit Notre Dame during April and May, 1948. This lecture series was established by Peter C. Reilly, a member of the Board of Lay Trustees and the Advisory Council for Science and Engineering, Notre Dame.

The University of California, Santa Barbara College, has recently created the Departments of Biological Sciences and Physical Sciences to replace the former Department of Natural Sciences. The new departments were established to facilitate the operation of the expanded science program and give recognition to growing emphasis in the liberal arts field. Elmer R. Noble, associate professor of zoology, has been appointed chairman of the Department of Biological Sciences, and Hazel W. Severy, formerly head, Department of Natural Sciences, has been appointed chairman of the Department of Physical Sciences.

The University of British Columbia has recently made the following new appointments in the Department of Physics: Kenneth R. More, Ohio State University, professor; John B. Warren, Department of Natural Philosophy, Glasgow University, associate professor; George L. Pickard, Operational Research Section, Royal Air Force, associate professor; A. Van der Ziel and A. J. Dekker, Phillips Laboratory, Eindhoven, Holland, associate professors; and G. G. Eichholz, Leeds University, assistant professor.

Illinois Institute of Technology has undertaken a \$34,000 two-year research project in conjunction with the U. S. Navy's continuous fight against corrosion. The new program will be supervised by Hugh J. McDonald, director of the Institute's Corrosion Research Laboratory. The problem will be to develop a more rapid and exact method of rating the chemicals which retard corrosion and to devise a numerical scale for expressing their worth.

Oklahoma Baptist University has moved its Biology, Geology, and Physics Departments into the new two-story W.

T. Short Memorial Science Hall, which was named in honor of the University's pioneer professor of mathematics and physical sciences, and completed in August. The removal of these three departments from Shawnee Hall has permitted an expansion of the Departments of Photography and Chemistry.

**Cornell University** will dedicate Savage Hall, new home of its School of Nutrition, on October 10 at a convocation on "Nutrition—A Key to Human Welfare." Speakers will include Thomas E. Dewey, governor, New York State; Clifford R. Hope, congressman from Kansas, and chairman, Congressional Agriculture Committee; W. H. Sebrell, National Institute of Health, Bethesda, Maryland; Frank M. Smith, chairman, New York State Conference Board of Farm Organizations; Leonard A. Maynard, director, School of Nutrition, Cornell; and Neal D. Becker, chairman, Cornell University Board of Trustees. Savage Hall, built and equipped with the aid of funds provided by New York State and by farmers of the Northeast, will provide the School of Nutrition with greatly enlarged facilities for teaching and research. The building is named for Elmer Seth Savage, professor of animal husbandry, Cornell University, an early leader in nutrition studies and a member of the faculty for 35 years until his death in 1943.

**Case Institute of Technology** has recently established a Research Laboratory for Mechanical Metallurgy, which occupies the newly constructed third floor of the Rockefeller Metallurgical Engineering Building on the Case campus. **George Sachs**, professor of physical metallurgy, has been appointed director of the new laboratory which will supplement the graduate instructional and research facilities of the Department of Metallurgical Engineering. The modern equipment of the laboratory makes it one of the most complete of its type in the engineering colleges of the country.

**The State College of Washington, Pullman**, has announced the following new appointments in the Department of Horticulture during the last six months; **Archle Van Doren**, formerly of Ohio State University, as associate professor and associate horticulturist, to investigate fruit handling and storage problems; **Edward Ross**, formerly of the University of California, as associate professor and

associate horticulturist, to investigate fruit and vegetable processing; **E. W. Kalin**, formerly of the University of New Hampshire, as assistant professor of floriculture and assistant horticulturist; **J. W. Caddick**, formerly of Cornell University, assistant professor of landscape gardening and assistant horticulturist; and **T. E. Randall**, formerly superintendent of the seed production laboratory, Mount Vernon, Washington, transferred to the State College as associate professor and associate horticulturist, to be concerned with horticultural breeding problems and cytogenetics.

## Meetings

At the 92nd convention of the **Electrochemical Society, Inc.**, to be held October 15-18 (*Science*, August 15), J. B. Fisk, director of research, U. S. Atomic Energy Commission, and E. D. Canham, editor, *The Christian Science Monitor*, will be the luncheon speakers. A dinner will be given in honor of Colin G. Fink, who has retired as secretary of the Society after 26 years of service.

**Brookhaven National Laboratory** will hold a Conference in Biology and Medicine on October 16-18. Subjects for discussion have arisen out of the many questions raised by scientists interested in the use of radioisotopes in medical and biological research. Topics include: "Legal Aspects in the Use of Radioactive Materials," "Protective Measures for Personnel," "Protective Measures for Public Health," "Evaluation of Procedures Used in the Examination of Individuals Exposed to Radioactive Materials," "Procurement of Isotopes," "Shipping of Isotopes," "Handling of Radioactive Materials," and "Disposal of Radioactive Waste Materials." There will also be a demonstration of radiation detection instruments.

Those interested in attending the Conference should communicate with Miss Ellen Matteson, Secretary, Conference Committee, Brookhaven National Laboratory, Upton, New York.

**The Surgeon General, U. S. Public Health Service**, has appointed an Advisory Board whose function is to designate the proper names for the several anti-Rh blood-typing serums licensed under the Biologics Law. The desire is to have recommended a system of nomenclature

which will be adequate to cover this phase of human genetics and which can be readily adapted to clinical use, medical teaching, and laboratory diagnosis. Members of the Board are: William B. Castle, Jr., professor of medicine, Harvard Medical School; Maxwell M. Wintrobe, professor of medicine and department head, School of Medicine, University of Utah; and Laurence H. Snyder, professor of medical genetics and dean of the Graduate School, University of Oklahoma.

At a Conference on Nomenclature of the Rh Factors, to be convened at 9:30 A.M., October 20, at the Hotel Statler, Washington, D. C., and continued through the 21st, the Board will be pleased to hear evidence from persons qualified in this field. Those having evidence to present should communicate in advance with: M. V. Veldee, Chief, Biologics Control Laboratory, National Institute of Health, Bethesda 14, Maryland. Others desiring to attend will be welcome, but advance notice of interest will be appreciated so that meeting accommodations may be assured. Copies of speakers' remarks, if extensive, are desired by the Board.

**The American Society for X-Ray and Electron Diffraction** and the **Crystallographic Society of America** on July 15 issued an invitation to the Crystallographic Union to hold its first International Congress in the United States late in the summer of 1948. Although no official answer has yet been received from the Union Committee, the response from individuals has been favorable, and plans are being made for the group to be accommodated on a small university campus, probably during the week of August 30-September 5.

## Recent Deaths

**Alice J. Rockwell**, 49, clinical psychologist, University of Maryland Medical School and Hospital, and Maryland Mental Hygiene Society, died September 3.

**Robert Nason Nye**, 55, associate pathologist, Boston City Hospital, and assistant professor, Harvard Medical School, died September 10 after a brief illness.

**William Gillespie**, 76, professor emeritus of mathematics, Princeton University, and a member of the Princeton faculty for 42 years before his retirement in



1939, died September 13 at his home in Princeton after a long illness.

Selig Hecht, 55, professor of biophysics, Columbia University, and a well-known authority in the field of vision, died September 18 of a coronary thrombosis at his home in New York City.

# COMMENTS

## by Readers

The British Association for the Advancement of Science, under the auspices of its Division for Social and International Relations of Science, on May 10 held a conference on "The Place of Universities in the Community." The following resolution, proposed by Sir Henry Dale, president of the Association, and passed unanimously, has since been approved by the Council: "This Conference recommends to the Council of the British Association that they should make representations to the competent authorities of all Universities of the British Commonwealth, urging that no contract should normally be accepted by the Scientific Departments of these Universities, if its terms include any restriction on freedom of publication."

Ludwig Silverberg remains unlocated in Europe. A recent search failed to disclose his whereabouts. Dr. Silverberg left Germany in 1936, and until recently his address has been "The Hague, Netherlands." Since further information is desired concerning some of his inventions, any assistance which can be given in locating Dr. Silverberg would be greatly appreciated. Communications should be addressed to: Reed Research, Inc., 1048 Potomac Street, N.W., Washington 7, D. C.

### Make Plans for—

American Public Health Association, October 6-10, Atlantic City, New Jersey.

American Association of Cereal Chemists, New York Section, October 7, 2 Park Avenue, New York City.

American Academy of Ophthalmology and Otolaryngology, October 12-17, Chicago.

American Association for the Advancement of Science, 114th Meeting, December 26-31, Chicago, Illinois.

This communication is written in the hope of opening a constructive discussion of the editing of scientific papers. That the subject deserves airing is certain from the continued grumbling we all hear and often swell. As editor of several journals and contributor to many more, I have both sinned and been sinned against. At the moment, several adventures in publication have put me more on the sinned against side, which prompts this note. It will be restricted to the problem of form; content is an independent subject.

Every journal is entitled to insist on certain style uniformities. If a certain spelling of a word (fiber rather than fibre) is preferred, if particular abbreviations are used or rejected (hr. for hour, but not % for percent), if a particular form of literature citation is demanded, the author who objects should submit his paper elsewhere. Good sense should prevent an unyielding application even of such rules—"Hrs. later conduction failed," or even, "After hrs. . .," would hardly do; but the editor is arbiter of usage. Further, no author will complain about correction of errors in spelling, punctuation, grammar, citation, fact (providing they are errors); and few, about suggestions of improved sentence structure, or organization, or even the nuances of style. But here the pendulum swings over, and the author, not the editor, has become final arbiter. The editor may only suggest.

An editor may properly reject a paper solely on the basis of obscure or verbose presentation, or may offer to accept it subject to improvement, or may generously detail the revisions demanded for acceptability and others recommended for improvement of the presentation. The decision is then the author's: to submit his paper elsewhere, to sweat over it further (perhaps with the aid of a more literate colleague), or to welcome the editor's proffered help and accept those revisions which seem good to him. There is one absolute essential in editor-author relations that I am saving for the "punch line"; with that operative, the balance indicated can work admirably.

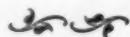
I know editors who have performed minor and major surgery on hundreds of manuscripts; who have, in special cases, as when highly important results were poorly presented, literally rewritten an article completely. (One condensed, by rewriting, a 75-page manuscript, by a man senior in age and achievement, into one of 23 pages.) And no anguished cries resulted. On the contrary, it was generally true that the more drastic the operation, the more grateful the subject. The reason? Adherence to the critical condition.

I know authors who have been awed to find an incorrect page number in an obscure reference questioned by the editorial office; who have been delighted to have headings of comparable tables recast into comparable form, and pleased to note correction of misspellings or of infelicitous constructions; who have been sadly tolerant, mostly, when commas have been deleted or adjectives substituted (for some sprinkle their commas and choose their words with considerable care, and the results are as intended); and who have been, sometimes, extremely annoyed when sentences have been recast, material omitted, style altered, meaning changed. Why annoyed? Because the critical condition was *not* always adhered to.

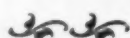
The editor should have final say as to what appears in his journal. The author should have final say as to what appears under his name. Between reasonable men agreement is readily attained, when adequate opportunity exists for exchange of reasons and preferences. In a case I know of, an invited article in a symposium on a highly controversial issue, the editor made many and serious changes from the original manuscript. The author restored the original form in galley proof and wrote a full explanation of his wish to retain his presentation. This letter was not acknowledged and some of the objectionable editorial changes remained in the published article.

By all means, have the editor "vet" each manuscript. Let him alter it to the best of his ability and his available time. Let him indicate which changes are demanded if

the article is to be accepted, which are judged highly desirable, which are minor suggestions. (All this is also applicable to content of an article, although this is less often altered.) And then, if any question of the acceptability of the changes to the author be possible, *insist that the edited manuscript, not proof, be returned early to the author for his consideration.* (R. W. GERARD, *Department of Physiology, University of Chicago.*)



**By the regulated action of sulfuric acid** paper is converted into vegetable parchment. Under similar conditions (occasionally in the presence of formaldehyde), cotton is transformed into a variety of Heberlein fabrics. Such treatment of other cellulose fibers, e.g. esparto, flax, jute, sisal, plywood (prior to folding), etc., would lead to a wide range of new materials possessing useful and attractive properties. Increased tensile strength, waterproofing, and general durability should add to the value of thread and plywood and result in a further development of textile and constructional material. In the case of wood, owing to its lignified condition, some preliminary treatment may be necessary, although not so drastic as that employed in the purification of wood pulp. The single fine layers of plywood should respond readily to such processing without impairing its original mechanical structure. (MAURICE COPISAROW, 1 Gildridge Road, Manchester, England.)



**Recent reports on the results of glucose tolerance tests** in vitamin-deficient animals (O. H. Gaebler and W. E. Ciszewski. *Endocrinol.*, 1945, 36, 227; A. Chesler, E. Homburger, and H. E. Himwich. *J. biol. Chem.*, 1944, 153, 219; S. Banerjee and N. C. Ghosh. *J. biol. Chem.*, 1947, 168, 207) do not refer to a series of papers published by McCay (D. McCay, *et al. Indian J. med. Res.*, 1916, 4, 1-27; 1918-19, 6, 485-549; 1919-20, 7, 22-80, 81-147). I came across McCay's papers fortuitously, and it seems probable that the later authors were not aware of the vast amount of work that had been done on human subjects at an earlier date. Nor have I been able to find any reference to these studies in

books, reviews, or textbooks that might be expected to mention the work. Since the studies were carried out with large numbers of patients and occupy several hundred pages of journal space, with many fully charted case reports, it is obviously desirable that they be called to the attention of modern nutritionists and physiologists.

McCay reported many cases in which patients who were losing 50 to 150 grams of glucose daily in their urine were made aglycosuric within 2 or 3 days. The patients were first restricted to a diet of milk, vegetables, and butter for a few days: "One to two pints of milk, 12-16 oz. of green vegetables, and 2 oz. of butter for 3 days will clear the urine of sugar and the blood of hyperglycemia in 99 per cent of all cases" (*Indian J. med. Res.*, 1919-20, 7, 81-147). The diet was then slowly built up until the caloric content was adequate, and eventually the patients were allowed to increase the rice in the diet. However, it was also stated that "in the treatment of diabetes in India the value of green vegetables cannot be too highly appraised."

One might surmise that the patients McCay studied were deficient in one or more vitamins. Certainly his findings should be confirmed or denied in terms of modern nutritional knowledge. If any assessment has, in fact, been made, no doubt others would like to hear of it. (VAN R. POTTER, *University of Wisconsin Medical School.*)



**Egg number is a matter of interest in fishery biology**, especially through its relation to mortality rates. The maximum usual number of ripe eggs in an individual of *Ostrea virginica*, estimated at 50,000,000-60,000,000 by W. K. Brooks (*Rep. Comm. Fish. Md.*, 1880, p. 14) and T. C. Nelson (*Bull. N. J. agric. exp. Sta.*, 1921, 351, 8), has more recently been placed at 500,000,000 by P. S. Galtsoff (*Science*, 1930, 72, 97-98). Computation of the volume represented by various numbers of eggs suggests that the order of magnitude of the later estimate may be too high.

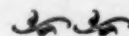
Galtsoff's value was based on an estimate of 115,000,000 eggs discharged at a single spawning. The gonad of this medium-sized individual was still 7 mm. thick after this discharge and was considered to contain sufficient ripe ova for

the spawning season's estimated four or five further periods of oviposition. However, 115,000,000 eggs 0.05 mm. in diameter (W. R. Coe. *Biol. Bull.*, 1932, 63, 428) would amount to a solid mass of about 8 cc. and would presumably require an ovary of about double this volume. From the data of C. Grave (*Rep. Shellfish Comm. Md.*, 1912, 4, 42) on cubic content of oysters, it would appear that Galtsoff's individual probably had a total body-volume of only about 15 cc. Therefore, it seems likely that the number of eggs discharged was miscalculated, perhaps by misplacing a decimal point.

A layer of gonad 7 mm. thick would be unusually great, since V. L. Loosanoff and J. B. Engle (*Bull. U. S. Bur. Fish.*, 1937, 33, 230) report a maximal average thickness of 9 mm. for any 6-oyster sample on any date and an average of only 4 mm. for 19 samples on the best date. The volume of a gonad 7 mm. thick in an oyster 3.7 inches long seems unlikely to have been as much as 10 cc., and the volume of packed eggs which it could have accommodated would probably not be as much as 5 cc. Therefore, if (as he evidently believed) Galtsoff's oyster had discharged only about one-fifth of its ripe eggs, the absolute quantity discharged might well have been only 0.8 cc., or 11,500,000, instead of 115,000,000.

The solid volume of a half billion eggs would be about 2 cubic inches. About 110 such masses would fill a gallon. Allowing for looser packing in the ovary and for the nonovarian content of the animal, it seems probable that an oyster of size to contain 500,000,000 eggs would be one of some 40/gallon at smallest. The largest recognized commercial category of oyster ("extra large") is defined at 160/gallon. Galtsoff's oyster was evidently a "select" of about 270 count.

It is, of course, possible that, by continued gametogenesis after the inception of spawning, an oyster might during a single season produce eggs in excess of its own volume. However, available reports do not make clear to what extent this might occur in *Ostrea virginica*, and this possibility was evidently not the basis of Galtsoff's estimate. (MARTIN D. BURKENROAD, *Survey of Marine Fisheries of North Carolina.*)





## Citrinin as an Antibiotic

YU WANG and F. K. HONG

Research Laboratories,  
Pincomb Chemical Works, Ltd., Shanghai

F. T. HWANG and C. S. FAN

The National Institute of Biological  
and Chemical Production, Shanghai

This is a preliminary report on bacteriologic, toxicologic, and therapeutic studies on citrinin begun by two of us in the Pincomb Chemical Research Laboratories in the early spring of 1945 and participated in by the group in The National Institute of Biological and Chemical Production beginning in 1947. The citrinin used in these experiments was isolated from the culture medium of *Penicillium citrinum* Thom, identified by G. Smith in England through the courtesy of J. Needham and found to be identical to that of Hetherington and Raistrick (2).

The study on bacteriostatic properties of citrinin was begun before V-E Day in complete ignorance of the work of Raistrick and Smith (4), Robinson (5), Oxford (3), and Ambrose and DeEds (1). The details of all these reports on antibiotic properties, with the exception of that appearing in the *Journal of Pharmacology*, are still not accessible to the authors. Table 1

TABLE 1

Species of bacteria	Gram stain	Minimum concentration of citrinin (mg./cc.)	Results
<i>Str. viridans</i> .....	+	0.05	Complete inhibition
<i>B. mycoides</i> .....	+	0.05-0.1	" "
<i>B. graveolens</i> .....	+	0.1	" "
<i>Staph. aureus</i> .....	+	0.4	" "
<i>Pneumococcus</i> .....	+	0.5	" "
<i>V. cholerae</i> .....	-	1	" "
<i>B. typhosus</i> .....	-	1	" "
<i>B. dysenteriae Flexner</i> .....	-	2-4	" "
<i>B. coli</i> .....	-	4	" "
<i>B. paratyphosus</i> .....	-	8	" "
<i>P. pyocyanea</i> .....	-	>15	Partial "

summarizes the results from our inhibition experiments with citrinin on bacterial growth.

For inhibition tests, 1 drop of a 24-hour bacterial culture was added to 1 cc. of ordinary broth medium containing different amounts of citrinin. After incubation for 16 hours, readings were taken. The figures in the third column represent the minimum concentrations of citrinin required for the complete inhibition of growth of different species of bacteria within 16 hours of incubation. It is evident that gram-positive bacteria are more susceptible to citrinin than gram-negative ones. *Streptococcus* and *Bacillus mycoides* are the most susceptible.

It is interesting to note that bacteria could be "sensitized" by citrinin so that their resistance was significantly reduced by

continuous subcultivations in media containing subminimal concentrations of citrinin. For instance, untreated *Staphylococcus aureus* required 0.4 mg./cc. of citrinin for complete inhibition, but after 10 treatments with citrinin ( $2 \times 0.1$  mg.,  $8 \times 0.05$  mg./cc.) it required only 0.05 mg., the time interval between two subsequent treatments being always 24 hours. The bacteria so treated resumed their normal multiplications immediately after being transferred into an ordinary broth medium. After 9 transfers in the broth, the descendants were still sensitive to citrinin, since 0.1 mg. of citrinin was already sufficient for their complete inhibition. Another instance is *Pseudomonas pyocyanea*. This could be inhibited by 4 mg. of citrinin after 9 subsequent subcultivations in a 0.4 per cent citrinin-broth medium, which was normally ineffective. The other bacteria (*Str. viridans*, *B. typhosus*, *B. dysenteriae*, *B. coli*, *B. paratyphosus*, and *B. mycoides*) behaved similarly.

Another remarkable finding was that the citrinin-treated staphylococci were also more susceptible to sulfadiazine. For example, those which were untreated required more than 5 mg. of sulfadiazine/cc. of medium for inhibition, while the "sensitized" ones needed 1 mg./cc. only.

Human serum (10 per cent) had no significant effect on the action of citrinin on *Staphylococcus*, *B. typhosus*, and *B. mycoides*. Cysteine (0.25 per cent) had no counteraction on citrinin. Sodium thiosulfate (0.5 per cent) and p-aminobenzoic acid (0.1 per cent) had no antagonistic action.

For toxicity tests we used albino rats and rabbits as experimental animals. For the rat the intraperitoneal lethal dose of citrinin was 1.7 mg./100 grams body weight, and for the rabbit, 5. mg. Autopsy showed hemorrhages in lungs and liver and accumulation of blood in the chest cavity. Repeated daily injections of citrinin in increasing doses resulted in increasing the tolerance of the animal to this substance. One rat (350 grams) was still living after receiving a total amount of about 155 mg. in 27 injections ( $1 \times 0.8$ ,  $5 \times 2.8$ ,  $8 \times 4$ ,  $5 \times 6$ ,  $4 \times 8$ , and  $4 \times 12$  mg.). A single intravenous injection of citrinin (2 mg./100 grams body weight) into the rabbit caused lacrimation, nasal discharge, salivation, drowsiness, and lowering of body temperature.

For therapeutic tests we have tried local application of citrinin on rabbits and human beings, and the results seemed very encouraging. In one experiment four rabbits of about 2 kg. were used. A piece of skin ( $1 \times 3$  cm.), together with some muscle beneath, was excised and the wound inoculated with *Staph. aureus*. After extensive pus formation two of the animals were treated locally with citrinin powder, one with sulfadiazine powder, the fourth, without any treatment, serving as a control. The citrinin-treated animals responded excellently. On the following day the lesions dried up, crusts formed, and in two days the wounds had healed. The sulfadiazine-treated rabbit showed some improvement, although some pus was still present on the fourth day of treatment. The control showed no improvement at all within 7 days.

Clinically, citrinin has been used in three cases of local infec-

tions, all of which showed dramatic results. The first had a cheek carbuncle with an indurated base inches in diameter; the second, an infected wound in the right palm; and the third, an ulceration with marked redness and induration over the chin and with enlarged and tender submaxillary lymph glands. The first two were staphylococcal infections; the last, streptococcal. Citrinin-sodium bicarbonate powder was applied locally to the infected region, and the indurated base was infiltrated with sodium-citrinin solution (1 per cent), after which it was dressed with citrinin-soaked gauze. At first, all experienced some needling pain but no other discomfort. The infected area dried up in 6-18 hours, the crust formation being followed by rapid healing.

The study on citrinin is still being carried on in the Pincomb Chemical Works along chemical, bacteriological, and clinical lines. The details of the above experiments will be published elsewhere.

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## *Lactobacillus acidophilus* Counts in the Saliva of Children Drinking Artificially Fluorinated and Fluorine-free Communal Waters<sup>1</sup>

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It has been demonstrated that there is a direct correlation between the number of *L. acidophilus* organisms in the saliva and dental caries activity in the mouth (3). In mouths with active dental decay the number of bacteria per cubic centimeter of saliva is high (20,000 or more), and in mouths in which the teeth are immune to decay at any specific time the counts are negative (under 100). Studies conducted by Jay (5) among representative population groups reveal that approximately 15 per cent of the individuals sampled have negative counts and about 57 per cent significantly high counts.

It has been established by Dean, *et al.* (4) that in areas in which fluorine occurs naturally in the drinking water supply there is a lower-than-expected incidence of dental decay among the group of the population studied (12- to 14-year-olds). In these fluoride areas, there is a much-greater-than-expected proportion of negative *Lactobacillus* counts (37.4 per cent) and a smaller-than-expected proportion of high counts (27.5 per cent) when the drinking water contains more than 1 ppm fluorine. The results of these *Lactobacillus* studies tend to confirm the dental findings.

<sup>1</sup> The media were furnished by the Division of Laboratories and Research, New York State Department of Health.

The authors wish to acknowledge the assistance of Mrs. Adele Polansky, statistician, and Miss Marion Guernsey, laboratory technician.

The purpose of this paper is to present a preliminary observation made in connection with the studies of *L. acidophilus* counts in the Newburgh-Kingston Fluorine Demonstration now being conducted by the New York State Department of Health (1, 2).

In order to determine the efficacy of introducing fluorine artificially into a public water supply for the purpose of reducing the incidence of dental caries, 1 ppm fluorine as sodium fluoride has been incorporated into the Newburgh water supply continuously since May 1945. Kingston, a comparable city, is consuming fluorine-free water and is being used for control purposes.

In Newburgh, individual *Lactobacillus* counts were made on random samples of the school population in 1944 and again in 1946 and 1947. The Kingston school population was sampled in 1946 and 1947. The findings are depicted in Fig. 1.

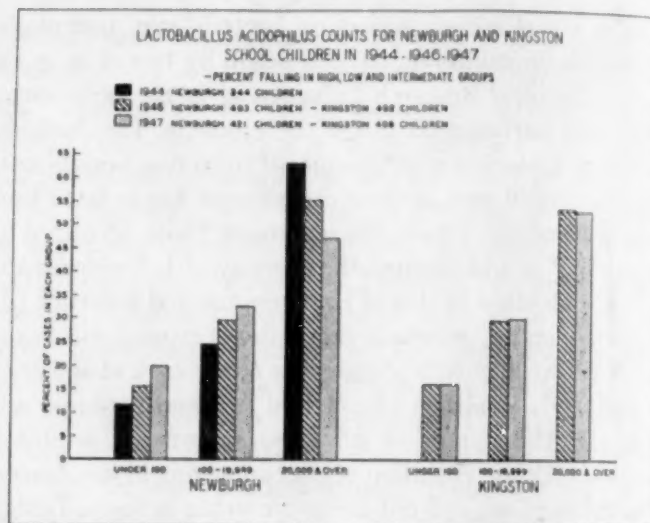


FIG. 1. *Lactobacillus acidophilus* counts for Newburgh and Kingston school children 1944-1946-1947—per cent falling in high, low, and intermediate groups.

Samples of saliva collected from 244 children of school age in Newburgh late in 1944 (prior to the introduction of fluorine into the municipal water supply), showed that 11.9 per cent were negative, and 63.5 per cent had counts of 20,000 or over. Analyses of salivas of 403 children in the same community early in 1946 revealed that there were 15.4 per cent negative counts and 55.2 per cent high counts. Of 421 samples collected early in 1947, 20 per cent had negative counts, while 47.3 per cent had high counts. In contrast, an analysis of the salivas of 402 children in Kingston early in 1946 revealed that 16.2 per cent had negative counts and 54.2 per cent, counts of 20,000 or over. In early 1947, among 408 children in Kingston, 16.2 per cent had negative counts and 53.9 per cent, counts of 20,000 or over.

It will be observed that while in Kingston the percentages of high and low counts remained approximately constant for the two-year period, there has been a consistent drop in percentages of high counts and a rise in the percentages of low counts in Newburgh since fluorination of the municipal water supply.

The standard significance tests were applied to the differences between the 1944 and the 1947 figures. The rise in the percentage of low counts (8.1 per cent) was 2.68 times its standard error, with a chance probability of .007. The drop in the percentage of high counts (16.2 per cent) was 4.03 times its standard error, with a chance probability of .00006. These differences may be considered statistically significant.



Although this is only a preliminary observation, it is in the direction which would be expected if artificial fluorination ultimately produces a decrease in dental caries.

Klein (6, 7) has recently shown, in higher fluorine concentrations, that a reduction in dental caries from fluorine can be a post-eruptive phenomenon. Since all the children examined in Newburgh drank water containing fluorine after many of their teeth had already erupted, the *Lactobacillus* counts bear on the controversial question of the effect of fluorine after eruption of the teeth.

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## A New Antibody in Serum of Patients With Acquired Hemolytic Anemia

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It has been possible to demonstrate an incomplete or "blocking" type of antibody in the sera from three patients (A. G., S. N., and L. H.) with acquired hemolytic anemia. None of these showed autoagglutination; one possibly showed auto-hemolysis. No significant titers of cold agglutinins were found. Donath-Landsteiner and Ham tests were negative. All had had splenectomy. One (S. N.) died; the other two have made some clinical and hematological improvement. Serum obtained prior to splenectomy was studied in one instance (A. G.).

TABLE 1  
IDIOPATHIC ACQUIRED HEMOLYTIC ANEMIAS

Test	Patients		
	A. G.	L. H.	S. N.
Autoagglutination.....	—	—	—
Panagglutination.....	—	—	—
Autohemolysis.....	—	—	+
Direct developing test.....	++++	+++	++
Pos. indirect developing tests.....	12	7	3
No. of indirect developing tests performed*	12	7	3
Titer of free antibody.....	1/4,096	1/256	1/128

\*Each test performed with type O cells from different individuals, both Rh- and Rh+.

Serum from rabbits immunized with human serum has been used to demonstrate the presence of the incomplete antibodies, both on the red cells and free in the sera of the patients. It has also been possible to trace the antibodies through several procedures which demonstrate some of their immunological properties. The testing (developing) serum prepared in a manner similar to that described by Coombs, Mourant, and Race, gave

a positive interphase precipitin test against human serum diluted 1/20,000 (2). A "direct developing test" is performed against thoroughly washed patient's cells. If the cells agglutinate on addition of the developing serum, the test is considered positive. The "indirect" test is performed in the same manner against appropriate normal cells which have first been incubated with the patient's serum. If agglutination occurs, it is presumed to constitute a demonstration of free antibody in the patient's serum (1, 3). A titration of the free antibody in the patient's serum can be made, using the indirect method, against cells sensitized in serial dilutions of that patient's serum. The actual developing test is done by the slide technique. Equal volumes of a 2 per cent sensitized cell suspension and the developing serum are mixed on a slide and allowed to stand for 5 minutes. Table 1 summarizes results common to all three patients. Table 2 lists comparable observations on control cases of hemolytic anemia.

TABLE 2  
CONTROL HEMOLYTIC ANEMIAS

	Hereditary forms			Erythroblastosis fetalis	
	Cooley's (2 cases)	Familial jaundice (2 cases)	Sick-lemia (1 case)	Patient (3 cases)	Mother (3 cases)
Auto- and panagglutination..	—	—	—	+-	—
Auto- and panhemolysis.....	—	—	—	—	—
Direct developing test.....	—	—	—	++	—
Titer of free antibody					
Rh+ cells.....*				1/32	1/512
Rh- cells.....				0	0

Further studies have been carried out with serum from case A. G. The titer of antibody in the presplenectomy serum was found to be 1/512, this serum having been stored at 4°C. for 6 months. The postsplenectomy titer is 1/4,096 in fresh serum. It has been possible to test the thermolability and species specificity and to investigate the relative position of the receptor for this new type of incomplete antibody. A high-titer saline

TABLE 3  
REACTION OF THE A. G. ANTIBODY WITH VARIOUS RECEPTORS

Receptor	Developing test
Type O cells	
Rh+.....	++
Rh-.....	++
Type B cells.....	++
" AB cells.....	++
" A cells.....	++
Rhesus cells.....	0*
Sheep cells.....	0†

\* Developing serum first absorbed with "unsensitized" rhesus cells.

† Sheep cells sensitized with human heterophile antibody have been found to give a positive developing test.

eluate (1/512 at 56°C., 1/32 at 37°C.) of the antibody from A. G. was prepared by incubating patient's cells or sensitized normal cells in equal volumes of saline for ½ hour at 56° or 37°C. Table 3 lists the reactions of this eluate with various receptors as brought out by the developing test.

Other observations of the A. G. serum have shown that the antibody cannot be demonstrated by the developing test to have reacted with red cells stored in normal saline solution for

several days. Type A, B, and AB cells, strongly sensitized in a saline eluate, react in the usual manner with  $\alpha$  and  $\beta$  isoagglutinins as specifically and intensely as prior to their being sensitized. Rh+ cells similarly sensitized likewise are not affected in the reactivity with Rh agglutinins. This is interpreted as showing that the A. G. antibody does not block the Rh and major blood-group receptors. This antibody is not reduced in potency at exposure to 70°C. for 10 minutes, but cannot be demonstrated by the indirect developing test after exposure of the serum to 80°C. for 10 minutes. As shown in the above tables, (in distinction to the Rh antibody) this antibody reacts with red cells irrespective of Rh type, is also an autoantibody and a panantibody, but does not react with rhesus cells.

Hematological, histological, and clinical data, as well as further immunological studies concerning these three patients will be submitted in greater detail in a future publication.

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### Further Observations on Leptospirosis in Micronesia

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Murine leptospirosis has given rise to a public health problem in many parts of the world (2) because the etiologic agent, *Leptospira icterohemorrhagiae*, also causes Weil's disease in man. Since the United States now has control of many islands in the Pacific, it seemed advisable to start work of a survey nature on these islands to find out whether leptospirosis constitutes a menace to the native peoples and our own personnel. Such investigation was started during the summer of 1946, when the University of Hawaii, in cooperation with the Navy, sent a number of biologists into the field.

In a recent report by Alicata (1), covering a part of the first summer's work, it was pointed out that 5 out of 40 rats trapped on Moen and Ponape, in the eastern Carolines, were infected with leptospirae. It is the purpose of this communication to note survey findings on the island of Yap, in the western Carolines. Yap, it will be remembered, lies south and west of Guam, about 9 degrees north of the equator. Prior to World War II it was one of the territories mandated to Japan.

A number of traps were put out near the site of the military government unit at Yap Town. The 28 rats which were taken alive were members of 3 species, *Rattus alexandrinus*, *R. norvegicus*, and a third, tentatively identified by Harvey Fisher, of the University of Hawaii, as *R. exulans micronesiensis*. Each animal was killed by drowning the morning after being caught, and a piece of kidney was removed at autopsy immediately after death. The tissue was preserved in 10 per cent formalin for several months before being sectioned and stained by a modification of the Warthin-Starry silver precipitation technic.

Careful microscopic examination of several sections from each rat kidney failed to reveal any spirochetes in the urinary tubules or elsewhere. Although the number of animals is small, it would seem that murine leptospirosis is not present

in the area studied. It may be that the geographic isolation of Yap and its lack of shipping facilities have prevented the introduction of *L. icterohemorrhagiae*. Once introduced into this region, which offers much rain and a large rat population, the organism might gain a foothold quickly.

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### Triphenyltetrazolium Chloride as a Dye for Vital Tissues

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The use of triphenyltetrazolium chloride as a test reagent for seed germinability was brought to the attention of one of us (R. A. D.) while on a tour of duty in Germany in 1945 as scientific consultant for the Technical Industrial Intelligence Branch of the Joint Intelligence Objectives Agency. The use of this compound for predicting seed germination was based on its ability to stain only those parts of seed embryos which were capable of growth. This fact suggested that the tetrazolium salt might have a wider application as a test reagent for the vitality of tissues other than seeds.

Tetrazolium salts, including 2,3,5-triphenyltetrazolium chloride, were first prepared by Pechman and Runge (5) in 1894. In 1941 Kuhn and Jerchel (2) synthesized a number of tetrazolium salts by an improved procedure and called attention to the fact that dilute solutions of 5-methyl- and 5-hendecyl-2,3-diphenyl salts stained yeast, garden cress, and bacteria (3). These workers believed that the reduction of the colorless salt solutions to a red compound which dyed the plant tissues was not due to the presence of glutathione, ascorbic acid, or cysteine, for the latter substances did not reduce these salts below a pH of 9.0, whereas the characteristic reductions observed on yeast, garden cress, and bacteria took place in neutral solutions.

As a result of these studies Lakon (4) substituted triphenyltetrazolium chloride for the toxic sodium selenite in his "topographic method" for testing the germinating ability of seeds. By a comprehensive series of comparative staining and germination tests he was able to show that it is possible to predict the germinability of corn, oats, rye, wheat, and barley by observing the embryo parts which are stained by the red, insoluble formazan deposited in viable tissues. The unstained portions of the embryo were shown to be incapable of growth.

Porter, Durrell, and Romm (6) used Lakon's tetrazolium method and found a close agreement between the percentage of stained embryos and the percentage of normal sprouts obtained in standard germination tests with corn, wheat, rice, buckwheat, popcorn, soybeans, and Bahia grass. Less satisfactory agreement was found in a comparison of the two methods when applied to vetch and sorgo and to some lots of oats, peas, and barley.

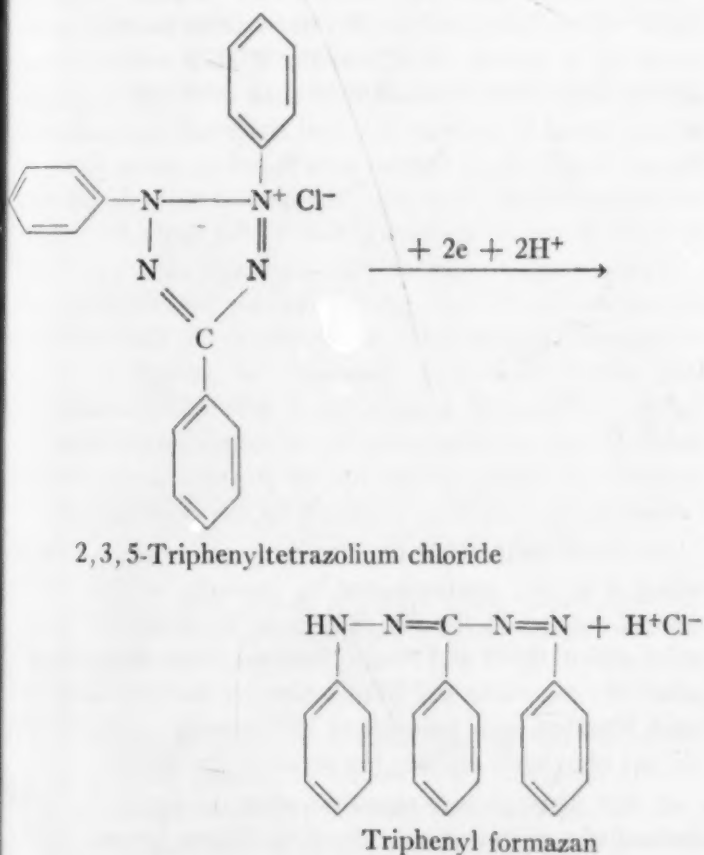
Since tetrazolium salts were not available in this country, we synthesized the triphenyl compound and the 5-furfuryl-2,3-diphenyl derivative and have used these compounds in preliminary studies on various types of viable and nonviable



tissues. The furfuryl derivative appeared to give the same tests as the triphenyl compound. In order to prepare tetrazolium salts of suitable purity in satisfactory yields, it was necessary to make certain modifications in the method of Kuhn and Jerchel. This phase of our work will be published later.

Our work also confirms the work of Lakon with seed corn and the observations of Kuhn and Jerchel with yeast. However, we have been interested in the potentialities of the tetrazolium salt as a test reagent for living tissues in general. We have found that many other viable materials, in addition to seeds and yeast, will reduce the triphenyltetrazolium chloride at pH 6.9: the fleshy parts of apples, oranges, and grapes; the gill area of mushrooms; carrot roots, white and sweet potatoes; young leaves; the stigmas and ovaries of certain pollinated flowers; bull sperm and the blastoderm of hen's eggs. Much to our surprise, the serum of bull sperm and the chalazae of egg white give a positive reaction. The reduction of the tetrazolium salt is not due to sugars, for subsequent work has shown that reducing sugars form the red formazan only above pH 11.0, whereas the above-mentioned materials will reduce the triphenyl compound at acidities below pH 7.0.

The use of the tetrazolium reagent should have a distinct advantage over many indicators as a viability test, since it is one of the comparatively few organic compounds which is colored in the reduced state. In the presence of viable tissue the colorless solution of triphenyltetrazolium chloride forms the insoluble red triphenyl formazan by the following reaction:



It is quite evident that enzyme systems are responsible when this reduction takes place in plant and animal materials, since tissues heated at 82° C. or higher lose their ability to reduce this salt. Furthermore, it is probable that this reduction is caused by dehydrogenase systems requiring coenzymes I or II, for Jerchel and Möhle (1) have shown that the apparent

redox potential of 2,3,5-triphenyltetrazolium chloride is about -0.08 volt. Thus, it is possible for this compound to act as an electron acceptor for many pyridine nucleotide dehydrogenases. We have found that one of these holoenzymes, glucose dehydrogenase-coenzyme I, in the presence of its substrate, reduces the salt at pH 6.6.<sup>1</sup> Work is being continued to determine if other enzyme systems possess similar properties when treated with this reagent.

Preliminary experiments have indicated that the enzyme systems responsible for the reduction of the tetrazolium salts are present in a wide variety of living tissues. In all probability, the reduction of these compounds by enzymes of living cells cannot be considered a general test for life. Nevertheless, the unusual properties of these reagents suggest that they might be utilized in many types of biological research involving differences in tissue viability.

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## Oxygen and Air Pressure Effects Upon the Early Development of the Frog's Egg

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The following constitutes a report on a part of the author's studies of the effects upon early embryological development of (1) different pressures of normal air and (2) various proportions of the constituent substances of normal air under pressure.

Eggs of three species of frogs (*Rana pipiens*, *R. sylvatica*, and *R. palustris*) were used in these observations. Two sets were employed: normal eggs deposited under natural conditions and, in the case of *R. pipiens*, pituitary-stimulated eggs from females brought in shortly before the breeding season and kept in a state of prolonged hibernation in a cold room at approximately 1° C. In the case of eggs deposited under natural conditions, the period of development during which experiment was initiated varied between the 4- and the 16-cell condition. The pituitary-induced eggs were placed in the pressure chambers 15-20 minutes after the sperm suspension was added. Eggs from two separate females and sperm from two males were used in each experiment.

Pressures up to 3 atm. of oxygen were added to the normal air pressure in the pressure chambers. Small egg masses were placed in small glass dishes and covered with water to a depth ranging from  $\frac{1}{8}$  to  $\frac{3}{8}$  inch above the surface of the mass. The water remained unchanged while the eggs were in the pressure chambers. Control eggs were kept in finger bowls or crystallizing dishes in shallow water which was changed daily. The control embryos were watched until they reached the late yolk plug and early neurulation state, after which the pressure

<sup>1</sup> We are indebted to F. A. Baldauski, who made the glucose dehydrogenase and coenzyme I preparations.

chambers were opened. The experiments were carried out at room temperature which ranged from 14° to 20° C., with the exception of two experiments on the induced eggs, where the temperature varied between 16° and 25° C.

The following results were obtained for naturally deposited eggs:

(1) Pressures of oxygen added as above have no apparent gross morphological effect upon development through the blastular stage.

(2) Increased pressures of added oxygen have an accelerative effect upon gastrulative and neuralative processes.

(3) Embryos subjected to treatment as above, removed from the chambers, and placed in finger bowls of shallow fresh water continued to develop as follows: (a) Up to 1½–2 atm. of added oxygen no apparent deleterious effects were observed in the tadpole condition. They may show acceleration in development compared with controls; (b) embryos experiencing 3 atm. of added oxygen develop various conditions of abnormal development in the tadpole stage.

(4) Compared with the controls, oxygen added under pressure approximating 1–1½ atm. appears beneficial to early frog development.

Comparison of development of pituitary-induced eggs of *R. pipiens* with that in normally deposited and normally ovulated eggs is under investigation. Thus far the results of experiments with eggs induced during the postbreeding season indicate a greater sensitivity to oxygen administered as above. The following general statements may be made:

(1) Pressures approximating 1 atm. of oxygen added to the normal air in the chamber accelerate development.

(2) Similar pressures produce a recovery effect in some of these pituitary-induced eggs. Comparison with controls demonstrates a greater number of normal-appearing neural fold conditions, with subsequent development into vigorous tadpoles in the oxygen-treated group.

(3) Pressures of added oxygen of 3 atm. suppress development at an advanced blastular condition. A few of these embryos may make abortive gastrulation attempts.

## Red Blood Cell Sensitivity to the Blood-Group-Enzyme

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The blood-group-enzyme, termed BGE, was first described by Schiff and co-workers (4), who considered it a physiological component of certain human secretions and excretions, being notably present in saliva and normal feces. The designation was adopted because these investigators found that the enzyme, independently of its source from an A, B, or O individual, acted on the blood group antigens of all the blood groups by destroying them. More recently, Schiff and Boyd (3) proposed the more inclusive designation "blood-group-property-destroying-factor."

Significant in relation to the present report is the statement

by Schiff and Akune (2) that this enzyme was not found in the brain or the blood serum.

The method of production of the BGE by the early workers consisted in inoculating a nutrient broth either with a saline extraction of normal nondiarrheal feces or with saliva (Sievers, 5) and then incubating the broth at 37° C. for 24 hours. By this procedure, the enzyme, which in the natural state is attached to either cellular debris or certain anaerobic bacteria, becomes enriched.

There was no evidence that BGE played any role in human pathology until 1941, when Neuda, in work done at the Pneumonia Laboratory of the Harlem Hospital, New York City, showed that the red cells of negroes suffering from sickle-cell disease developed sickle cells in from 10 to 30 minutes (at times much more rapidly) when suspended in a fluid medium prepared by the Schiff method and presumably containing the BGE. The preparation of the test fluid and the test itself were described by Neuda and Rosen (1) in 1945. In this paper, reasons were enumerated which suggest that Schiff's blood-group-enzyme might be identical with, or closely similar to, the sickle-accelerating substance. Whether or not this assumption is correct can be established only by future investigation. At the present stage of the work, however, this preliminary assumption seems appropriate as a working hypothesis. There are already further evidences at hand which point in the same direction. There remains the outstanding fact that a fluid produced by the Schiff method will rapidly reveal the presence or absence of the sickling quality if red blood cells obtained from a negro are suspended in this fluid.

Observations made since the previous paper appeared, which will be published shortly, have demonstrated that the sensitivity of human red cells to the BGE is not restricted to sickling negro cells. Essentially similar intermediate changes as were found to precede the final sickle-cell configuration in the red blood cells of negroes were found to occur also in red cells derived from Caucasians. The final twisted cell silhouette, however, remained a characteristic of the negro red cell.

This observation led to the conclusion that the possible damage to the red cells by this enzyme fluid might be more widespread than in sickle-cell disease alone. We have therefore coined the phrase "hemolysis of sickle-cell type" to signify this peculiar kind of blood destruction, and the expression "red cell sensitivity to the blood-group-enzyme" to indicate the liability of any red cell to react in characteristic fashion to the substance produced by the Schiff method.

The Schiff method has the disadvantage of using a material which is greatly contaminated by bacteria, so that the resultant changes in the red cells could be attributed to bacterial action. Schiff and Akune, however, have disproven this possibility regarding the BGE action by demonstrating that rigid filtration with removal of the bacteria weakened, but did not completely abolish, the action of the BGE.

A first attempt was therefore made to apply the Schiff method of enrichment by culture to plasma (or serum) of a sickle-cell case. This was done by pipetting about 2 cc. of sterile plasma (or serum) into 25 cc. of sterile nutrient broth, the mixture being corked and incubated at 37° C. for 24 hours.

This plasma(serum)-broth mixture developed the same sickle-accelerating substance as was originally produced from feces. The same procedure was successful in four more cases suffering from the following diseases: hemolytic jaundice,



ulcerative colitis, pernicious anemia, and cancer of the breast (postoperative).

The observations were carried further, and it was found that occasionally fresh plasma of certain individuals would produce the sickling effect on red cells directly, without the process of enrichment by culture. This was observed in two cases of cirrhosis of the liver, two cases of toxemia of pregnancy, and one case of myelogenous leukemia.

TABLE 1

Schiff's enzyme	Diagnosis of cases	No.
In plasma (serum)-broth	Sickle-cell disease	1
	Hemolytic jaundice	1
	Ulcerative colitis	1
	Pernicious anemia	1
	Cancer of the breast	1
	Cirrhosis of the liver	2
In natural plasma	Toxemia of pregnancy	2
	Myelogenous leukemia	1
Total.....		10

A total of 10 cases have revealed, by two different methods, the presence of the sickle-accelerating substance in blood plasma, a substance which, using Schiff's method, was found originally only in feces and saliva (Table 1).

It appears therefore, that the sickle hemolysis-inducing sub-

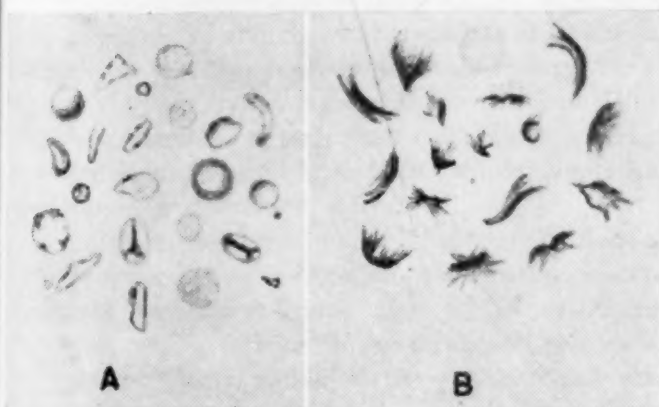


FIG. 1. Jackson washed red cells: A in saline, B in an enzyme broth prepared from feces. The first characteristic figures in B were seen in 8 minutes. The drawings were made after 1 hour.

stance, presumably BGE, or a substance closely related to it, is occasionally present in human blood under conditions still to be studied, and that it exists in two forms (demonstrable by the sickling test on the slide): one, less active but enrichable by culture procedure; the other, highly active as shown by the direct test.

The appearance of the red cells in the test is clean cut. The successive changes in shape from the normal round form of the red cell to the fine and delicately bent figures occur rapidly, and their occurrence is indicative that "red cell sensitivity to the blood-group-enzyme (Schiff's substance)" is present.

The necessity for additional studies in this field is emphasized. Further investigation of the significance of the occurrence of this sickle-accelerating substance in human disease is in progress.

The rapid sickling of the red cells obtained from two negroes, in the enzyme-containing media, is shown in Figs. 1-3. Jackson suffered from sickle-cell anemia, while Eddy had the sickling condition without anemia. Both were chosen

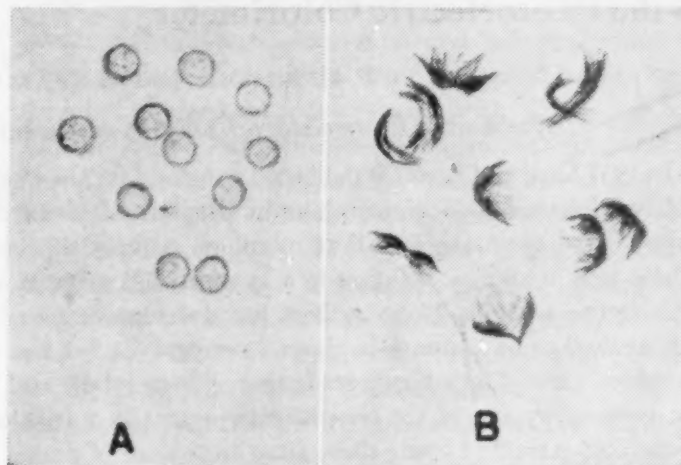


FIG. 2. Eddy washed red cells: A in saline, B in an enzyme-containing natural plasma (from a case of cirrhosis of the liver). The first characteristic figures in B were observed after 20 minutes. The picture was drawn after 1 hour.

because of their O blood group, to avoid any interference with the group antibodies when plasma was added.

The development of the successive changes in enzyme-sensitive sickling red cells, leading to the so-called "sickle,"

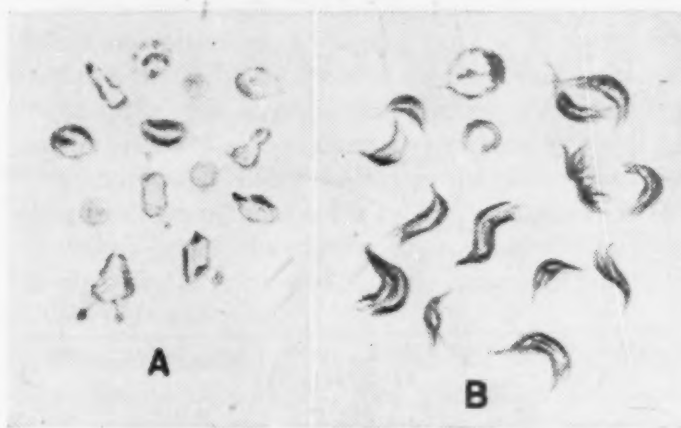


FIG. 3. Jackson washed red cells: A in saline, B in an enzyme-containing plasma (from a case of toxemia of pregnancy). The first characteristic figures appeared after 30 minutes. The drawing was made after 6 hours.

is characterized by many distinctive features which will be described in detail later.

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## Adaptation of the Silicomolybdic Acid Method for the Estimation of Morphine to the Photoelectric Colorimeter

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In 1937 Snell and Snell (2) published a method for the quantitative determination of morphine in tissues and biological fluids, based upon the fact that morphine reduces silicomolybdic acid in alkaline solution to a blue product suitable for colorimetric analysis. These authors found determinations by this method to be accurate to about 2 per cent for 2-7 mg. of morphine. One of its advantages is that silicomolybdic acid is not reduced by any of the constituents present in a trichloroacetic acid extract of tissue slices after incubation (1).

We have modified and adapted this method for use on a semimicro scale with the Evelyn photoelectric colorimeter. A strict proportionality is obtained up to 0.7 mg. of morphine, with only slight deviation from a linear relationship above this amount.

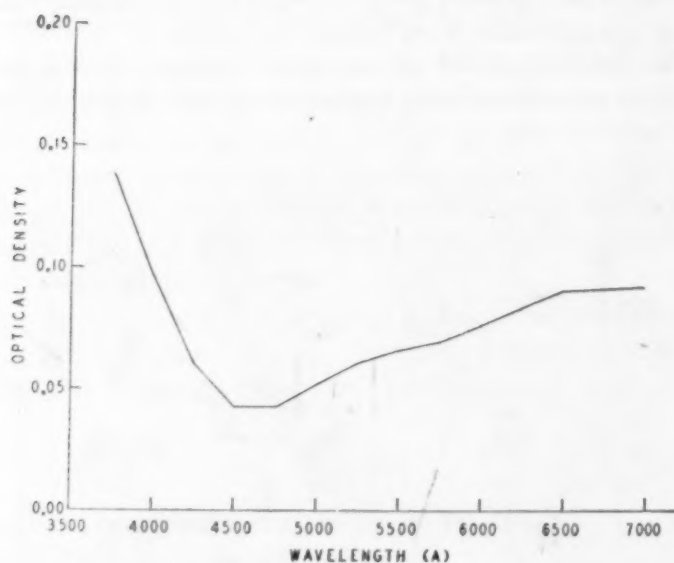


FIG. 1

A standard curve is obtained by introducing various amounts of morphine sulfate (0.1-1 mg.), in 5 cc. of distilled water, into 25-cc. volumetric flasks. This can be accomplished by adding various amounts (0.5-5 cc.) of 0.02 per cent morphine sulfate  $\cdot$  5  $H_2O$  to the flasks, followed by that amount of distilled water necessary to make a total of 5 cc. Next, 4 cc. of silicomolybdic acid reagent, prepared according to the method described by Snell and Snell, is added to each flask, followed by 0.5 cc. of 5 per cent trichloroacetic acid. Finally, 10 cc. of 5 per cent ammonium hydroxide is added. A reagent blank in which morphine is omitted is also prepared. The volume is diluted to 25 cc. with distilled water, shaken vigorously, and allowed to stand at room temperature for 25 minutes. It is then transferred to colorimeter tubes and read on the Evelyn photo-

electric colorimeter, using the 10-cc. aperture and a No. 660 filter. The reagent blank is used to obtain a center setting. Spectrophotometric study showed a plateau of maximum absorption, in the visual range, between 6,700 and 7,000 Å. (Fig. 1), with a possible peak in the ultraviolet which could not be investigated with existing facilities. Filter No. 660 has transmission limits at 635-720  $m\mu$ . L (photometric density) plotted against the amount of morphine sulfate present in milligrams (Fig. 2, A).

Recoveries from tissues incubated with morphine were also carried out, using more than 0.5 cc. of 5 per cent trichloroacetic acid (per 25 cc. total volume) to stop enzymatic activity; recoveries ranged from 93 to 110 per cent. However, 0.5 cc. of this reagent seems to be optimal for good linearity above 0.5 mg.; it is therefore suggested that, in recoveries of morphine from tissues, enzymatic activity be stopped by some other pro-

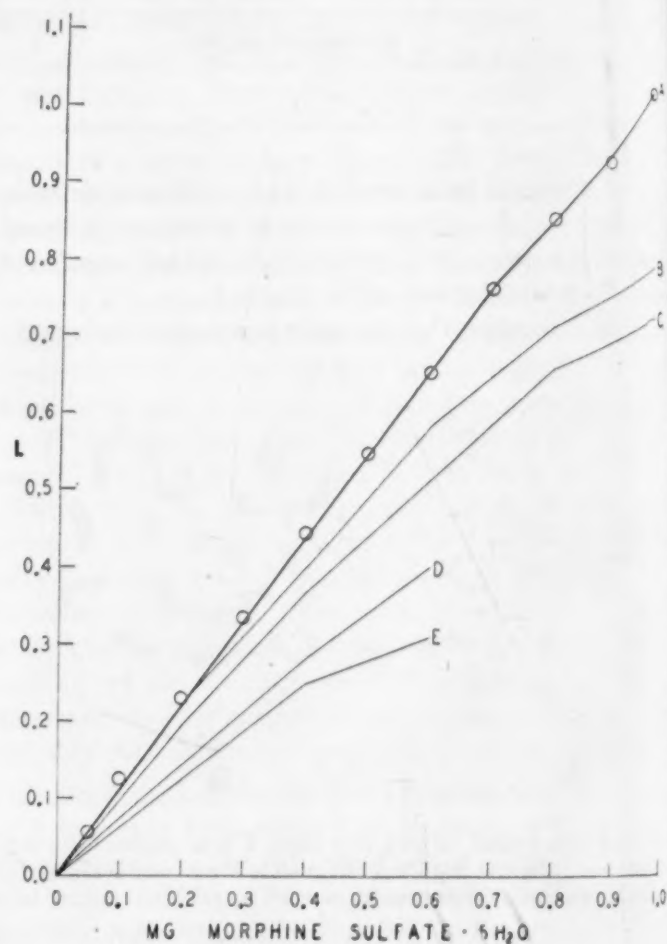


FIG. 2

tein precipitant, rather than by adding more than the optimal amount of trichloroacetic acid.

Some attempts were made to determine the mechanism of the specific action of trichloroacetic acid in increasing the sensitivity of the method and the range of the determination. It was found that the pH of the final solutions, prepared as outlined in the method and containing 0.5 cc. of 5 per cent trichloroacetic acid, was 9.94-9.98. This final pH was reproduced by substituting, for the trichloroacetic acid in the solutions being deter-



mined, sufficient amounts of 5 per cent acetic acid (Fig. 2, E), 0.1 N hydrochloric acid (D), 5 per cent monochloroacetic acid (C), and 5 per cent dichloroacetic acid (B), respectively. The ability of these acids to increase the sensitivity and range of this method decreased in the following order: trichloroacetic, dichloroacetic, monochloroacetic, hydrochloric, and acetic acid. This would suggest that the specificity of trichloroacetic acid in affecting this method is a function of the number of chlorine atoms attached to the carbon adjacent to the carboxyl group and not a matter of pH or the acetate radical itself.

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## Use of Phenol Formaldehyde and Vinyl Resins in Sealing Liquid Mounting Media on Microscope Slides

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A persistent difficulty in the preparation and preservation of certain types of plant materials on microscope slides is the problem of permanently sealing liquid mounting media. Glycerin, lactic acid, lactophenol, and certain other mounting fluids of diverse composition are exceedingly difficult to inure against changes in atmospheric humidity, temperature, and slow chemical reaction with the sealing agent. The dependence upon liquid media for mounting certain plant tissues, although unfortunate, is necessitated by requisite indices of refraction and other physical and chemical properties of diverse mounting fluids. It therefore becomes necessary to employ a sealing compound which gives a reasonable promise of permanence if extensive collections of such plant materials as pollen grains, leaf cuticles, fungus mycelia, and other whole mounts are to be maintained for permanent reference.

Recently, in the preparation of reference collections of root and leaf epidermal tissues for use in the identification of plant fragments in peat and lignitic coals, a need was realized for permanent sealing of glycerin and lactic acid preparations of such tissues. Consideration of the physical and chemical behavior of various synthetic resins and plastics indicated the possibility that phenol formaldehyde and vinyl resins might provide the necessary physical properties and chemical resistance. Preliminary tests showed a p-phenyl phenol formaldehyde resin and a vinyl acetate resin to be very promising for prolonged sealing of noncorrosive and certain corrosive media. These resins, when applied copiously with a brush or pipette to clean glass surfaces, form an effective seal which is not altered by prolonged storage at normal temperatures. In the case of the phenolic resin an accelerated aging test involving 8 months storage at 50° C. with frequent intermittent changes to room temperature has resulted in perfect sealing of lactic acid and glycerin preparations. The vinyl resins have not been subjected to as rigorous tests, but appear to be equally effective.

The phenolic resin showing the most desirable properties for a sealing agent is a p-phenyl phenol formaldehyde compound containing tung oil and a metallic soap as oxidizing agent. The

resin is prepared and sold as a commercial varnish and has the syrupy consistency of a thick oil. The setting of the liquid to a solid is complex chemically, involving solvent evaporation, oxidation of the tung oil, formation of colloidal systems, and polymerization of the resin. The dried and polymerized resin is exceedingly hard, yet slightly elastic, shows extreme adhesiveness to glass, and is extraordinarily inert chemically. When cured by drying and especially by heating to about 50° C., the resin is completely inert to ordinary organic solvents such as alcohols, hydrocarbon solvents, and halogenated hydrocarbons. Resistance to mineral acids was tested by ringing lignin residues of wood sections prepared with 72 per cent sulfuric acid. The resin shows effective sealing of the strong acid after 3 months storage at 40° C. A slight carbonization at the edges of the cover glass occurred shortly after sealing, presumably by action on the tung oil. In the case of organic acid media such as lactic acid and lactophenol, clouding of the resin may occur near the interface with the mounting fluid. This cloudiness does not appear to progress after polymerization of the resin at 50° C., and no tendency has been observed for the mounting fluid to become cloudy by emulsification of the sealing agent, as is frequently the case with compounds such as Noyers cement after prolonged storage.

For best results the p-phenyl phenol formaldehyde resins should be kept in a large stock container of quart capacity or more and drawn off only when needed. Small portions of the liquid resin, when kept in dropping bottles or similar containers, set to a gel within a day or two and are useless after jelling since the material becomes insoluble in organic solvents. When still liquid, the resin may be thinned with neutral xylene or ethyl acetate. The tendency to gel after exposure to air can be obviated by proper handling.

Slides, after ringing with the resin, may be dried for 8-24 hours and placed on a warming table or in an incubator to complete the polymerization of the resin. Some change in the color of the resin accompanies polymerization, resulting in an amber yellow. The resin shows no wrinkling by shrinkage after slow drying and polymerization on the glass. Clean glass surfaces are essential for perfect sealing, although excess glycerin or other liquid at the edges of the cover glasses may be effectively sealed if it is not sufficiently copious to form a film between resin and glass.

Phenolic resins of the type described here are produced by the Bakelite Corporation, New York City. The commercial product used in the writer's laboratory is prepared by the Brooklyn Varnish Company under the trade name of Tufon #74.

The vinyl resins tested as sealing agents showed great variation in physical properties and resistance to mounting media. Their advantages are ease of solubility in a wide range of organic solvents and clear, glass-like appearance. A vinyl acetate resin (Bakelite Corporation No. AYAF) proved most useful as a sealing compound, although its texture, chemical inertness, and adhesive properties are inferior to phenolic resins. It may be dissolved to desired viscosity in 95 per cent ethyl alcohol, butyl acetate, dioxane, ethylene dichloride, and other organic solvents. The vinyl acetate polymer appears to be inert to glycerin. The solubility of certain vinyl resins in ethyl alcohol containing as much as 50 per cent water suggests its use in the preparation and embedding of whole mounts of plant and animal tissues in which complete dehydration should

be avoided. Vinyl acetate resins are thermoplastic and remain somewhat flexible at room temperature.

Brief experience with the physical and chemical properties of certain industrial plastics has suggested that many other uses for such compounds may be found in histological techniques adapted for plant tissues. Reliance on the tried and true methods need not be sacrificed in the development of these new techniques or new materials for older techniques.

## An Effective and Nontraumatic Method of Handling Monkeys

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A technique which we use for catching monkeys preparatory to administering anesthesia has attracted sufficient favorable comment from monkey handlers who have witnessed its operation to warrant a brief note.

The two essential items of equipment are (1) the transport cage and (2) the square-hoop net, illustrated in Fig. 1. The

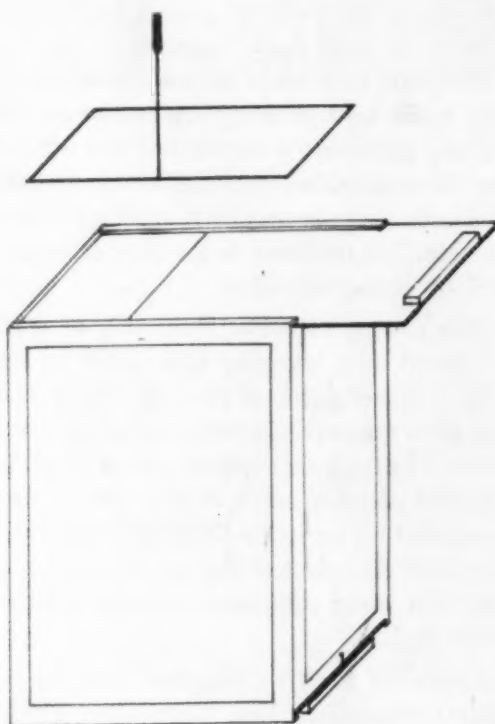


FIG. 1

transport cage, which measures 13 x 16 x 20 inches, is equipped with a sliding door on each end; its sides may be made of wire mesh to facilitate observation. The hoop of the net is constructed of  $\frac{3}{4}$ -inch rod. Its size (10 x 13 inches) is such that it fits easily into the transport cage.

The first step in the procedure is to chase or lure the monkey into the cage. This can be accomplished with surprising ease, for rhesus monkeys, after a little experience with the cage, react to it almost as though it were a haven of refuge. Once the animal is inside, the cage is set on end. The net is then placed in position over the sliding door, which is now on top. When the door is withdrawn, the net is moved down over the monkey. The lower door is then withdrawn and the hoop held against the floor. When the cage itself is lifted off the net, the enmeshed monkey lies helpless at one's feet.

The entire procedure is tolerated with a minimum of emotional upset for both monkey and man. Using this technique, a single unassisted worker can carry out intraperitoneal or subcutaneous injections. The various uses to which the method may be put are self-evident.

## Preservation of *Plasmodium vivax* by Freezing

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There are several methods of fever therapy for neurosyphilis, but induced malaria, either alone or combined with other agents, remains the method of choice of many syphilotherapists. A serious limitation to the more general use of malaria therapy has been the difficulty of providing a constant, readily available source of parasites. Plasmodia do not remain viable in blood under the usual conditions of storage (room temperature and icebox) for more than a few days (4). Preliminary results of preserving *Plasmodium vivax* by low-temperature freezing suggest that this may prove a practical method of long-term preservation.

Preservation of protozoa by freezing is not new. Turner (5) was able to maintain *Treponema pallidum* and *pertenuis* in a viable state at low temperatures for long periods of time. Coggeshall (1), studying human, avian, and monkey malaria parasites, reported failure with a process involving rapid freezing at  $-72^{\circ}$  to  $-80^{\circ}$  C. and slow thawing, but when thawing was effected rapidly, monkey parasites were preserved successfully for as long as 70 days. Others (2, 3, 7) have been able to preserve the various parasites of bird malaria at temperatures of  $-50^{\circ}$  to  $-70^{\circ}$  C. for long periods of time. Recently Weinman and McAllister (6) have reported the freezing and prolonged storage of several types of pathogenic human protozoa with conservation of virulence. Although human plasmodia were not studied, the preservation of *P. lophurae* in the frozen state for long periods was confirmed. Russell (4) has alluded vaguely to low-temperature freezing of human malaria parasites as a means of preservation for use in therapeutic malaria, but provided no documentation.

Since we have been unable to find reports of preservation of human plasmodia by freezing techniques, we wish to record the successful transmission of malaria to three subjects by inoculation of blood infected with *P. vivax* which had been frozen and maintained at low temperatures for periods of 10-15 days.

The donor from whom the strain of parasites was originally obtained was H. K., a veteran of service in New Guinea, who had been suffering from recurring attacks of vivax malaria. At the time of bleeding, blood smears showed many young ring forms of *P. vivax*; a rough estimate of parasite density was approximately 10,000/mm.<sup>3</sup>. Twenty cc. of blood was withdrawn into 3 cc. of 4 per cent sodium citrate solution, of which 10 cc. was immediately injected intravenously into D. M., a neurosyphilitic receiving penicillin therapy. Five cc. of the remainder was transferred to a thin-walled glass test tube and rapidly frozen at a temperature of  $-75^{\circ}$  C. by immersion in alcohol-dry ice mixture, the tube being rotated by hand until



the blood became solidified. The tube was then transferred to a dry-ice box for storage at approximately  $-50^{\circ}$  to  $-70^{\circ}$  C. Fifteen days later the frozen blood was thawed by immersion in a water bath at a temperature of  $40^{\circ}$ – $42^{\circ}$  C., and 4 cc. was injected intravenously into patient L. H. Ten days later this recipient of the preserved parasites developed a (rectal) temperature of  $40^{\circ}$  C., and blood smears showed ring forms of *P. vivax*.

Patient D. M., who had received 10 cc. of infected blood directly from H. K., the original donor, developed a paroxysm 40 hours after inoculation, and many ring forms of *P. vivax* were found in the peripheral blood. After several paroxysms, when the parasite count was approximately 5,000/mm.<sup>3</sup>, blood from D. M. was withdrawn into citrate. Approximately 2–3 cc. of this citrated blood was transferred to each of several small pyrex glass test tubes, which were closed with cork stoppers; and, as before, the blood was frozen by immersion in alcohol-dry ice mixture, then transferred immediately to a dry-ice box for storage. After a 10-day period of storage this blood was thawed, again by immersion in a water bath at a temperature of  $40^{\circ}$ – $42^{\circ}$  C. Several tubes which cracked during either freezing or thawing had to be discarded. About 4 cc. of the remaining thawed blood was injected intravenously into patient V. V., who on the 9th and 10th days after inoculation developed a low-grade fever with peaks of  $37.8^{\circ}$  and  $38.0^{\circ}$  C., respectively, but parasites were not demonstrated until the 11th day, when the patient had a shaking chill with fever of  $41^{\circ}$  C.

After two more paroxysms, the parasite density having risen to approximately 1,500/mm.<sup>3</sup>, V. V. was used as donor for the third experiment. The bleeding, anticoagulant, and freezing process were carried out in the manner previously described, with the exception that small, plastic, screw-capped vials were employed as containers. Freezing and transfer to the storage compartment were completed within  $\frac{1}{2}$  hour after bleeding. Fifteen days later the preserved blood was rapidly thawed (as before) and 6 cc., the contents of two vials, inoculated intravenously into each of two neurosyphilitics receiving penicillin therapy. After an interval of 9 days one recipient (E. M.) had onset of periodic episodes of chilliness, headache, and malaise accompanied by slight rises in temperature (maximum,  $38.1^{\circ}$  C.). The occurrence of this symptom complex followed a tertian pattern, but plasmodia were not demonstrated until the 19th postinoculation day, thick films having been negative on the 10th, 15th, and 17th days. On the 20th day a paroxysm occurred with elevation to  $39.4^{\circ}$  C.

Removal of the second recipient from the hospital during the incubation period terminated observation. The result of this inoculation is therefore not known.

It should be noted that the freezing and thawing process resulted in almost complete hemolysis of the red blood cells and that the staining characteristics and morphology of the parasites were considerably altered. Of three patients inoculated successfully, one recipient of the hemolyzed blood had a mild chill immediately after injection, with fever to  $38.0^{\circ}$  C., one had no apparent reaction, and one suffered a simultaneous febrile Herxheimer reaction (penicillin) which masked any unfavorable effect of the inoculum.

Many factors which may influence the success or failure of preservation of human malaria parasites by freezing remain to be studied. Among these are the age of parasites when frozen, the speed of freezing and of thawing, the temperature range

during storage, and the anticoagulant used. Studies are continuing to determine the effects of altering these variables, with the objective of developing a practical, reliable method of preserving human plasmodia for long periods.

It is suggested that this method may be used to provide a blood bank of malaria parasites for use in malaria therapy of neurosyphilis, and for preserving strains of human plasmodia for experimental purposes.

*Addendum.* Since this report was submitted for publication, three additional patients have been inoculated successfully with blood containing *P. vivax* preserved by freezing. In one instance, the blood had been frozen for 37 days.

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## Intraneural Bipolar Stimulation: A New Aid in the Assessment of Nerve Injuries

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Clinical observation may sometimes lead to erroneous conclusions concerning regeneration in peripheral nerve injuries. Such instances occur when a patient, despite neurotization of a muscle, remains incapable of voluntary movement or, conversely, when overlap innervation by a neighboring nerve seems to give evidence of regeneration although the nerve in question is actually interrupted.

The extent of regeneration of a nerve may often be clearly ascertained by surgical exploration, with electrical stimulation of the exposed nerve and observation of the reaction in its muscles. A means of obtaining such evidence without an operation has been devised.

Normal peripheral nerves may be excited by electrical stimulation through the intact skin. However, to excite the much less irritable regenerating nerves, stimulation over the skin (or with one electrode within the nerve) must be of such intensity as to result in mass contractions of adjacent muscles. This spread can be avoided and a small stimulus made effective if the current density about the nerve is increased by inserting both electrodes into or near the nerve.

Two sterile #25 hypodermic needles are introduced through the prepared skin, separated by a distance of 1–2 cm., into or close to the nerve in its longitudinal axis. A site of stimulation can be so chosen as to be proximal to the muscles in question and still at an area where the nerve is well defined in its position by surface topography. An effective stimulus is afforded by applying to the two needles a current of less than 5 milliamperes. Alternating and direct currents are equally satisfactory. Any of the usual stimulators may be used; in fact, even the make-brake stimulus delivered by a  $1\frac{1}{2}$ -volt dry cell in an adjusted flash-light is sufficient. The current is gradually increased until a

maximal contraction is obtained in the innervated muscles. The strength of contraction is estimated or measured. In the absence of motor response the presence of some regenerating nerve fibers at the point of stimulation is indicated by a tapping or burning sensation projected into the skin distribution of the stimulated nerve. If no sensory effect can be elicited, one may assume complete absence of regeneration only after having varied the position of the needles several times to preclude the possibility of poor contact with the nerve.

Intraneural bipolar stimulation has been carried out on over 1,000 patients at Cushing General Hospital during 1945 and 1946. Positive responses were followed by the return of voluntary contraction of variable degree. The absence of response could be confirmed, in most instances, by stimulation of the exposed nerve at the subsequent operation performed because of this finding. The first appearance of muscle contraction on intraneural stimulation permitted calculation of a mean nerve-growth rate of 1.4 mm./day. Long-term follow-up studies have shown that when, in a given patient, the schedule for beginning contraction of various muscles, predicated upon this growth rate, was not maintained within narrow limits, appreciable recovery of function could not be expected by further waiting.

Intraneural stimulation is an objective and easy means of discovering the extent of spontaneous or postsutural regeneration in an injured nerve. Needless surgery is avoided, and necessary surgery is anticipated because of the possibility of determining with greater accuracy and at an earlier time the presence or absence of adequate nerve regeneration.

## Interlaboratory Comparison of Measurements of $I^{131}$

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Radioactive iodine,  $I^{131}$  (8.0 days), is coming into use in increasing quantities in medical research and clinical treatments. It is desirable to have quantitative measurements of this material which are reasonably accurate for many of the purposes for which this isotope is used. Since quantitative procedures for measurements of this type are still in a developmental stage, many of the users as well as the producers have requested some form of intercomparison to determine how accurately measurements are made at present, with the aim of discovering and correcting any serious disagreements.

As a first step in this program the National Bureau of Standards procured a sample of  $I^{131}$  from the Clinton Laboratories and prepared from it a number of identical 25-ml. samples which were distributed to approximately 40 hospitals, universities, and similar institutions using this isotope or interested in its measurement. They were requested to measure this sample, which was approximately 1 rutherford ( $10^6$  disintegrations/second) total activity, and to report the results. Replies were received from 30 of these institutions, 26 of which reported results in terms of disintegrations per second. The remaining 4 gave values in counts per second, which could not be interpreted in terms of disintegration rates.

The reported values, plotted in Fig. 1, give some idea of the spread. One value was very high (nearly 100 times the average of the others), which seems to indicate an error in reporting

rather than measurement. Neglecting these values, the average value reported was  $3.0 \times 10^4$  disintegrations/second/ml. of 0.75 rutherford for the 25-ml. sample. The lowest value deviated from the average by 40 per cent and the highest by 80 per cent.

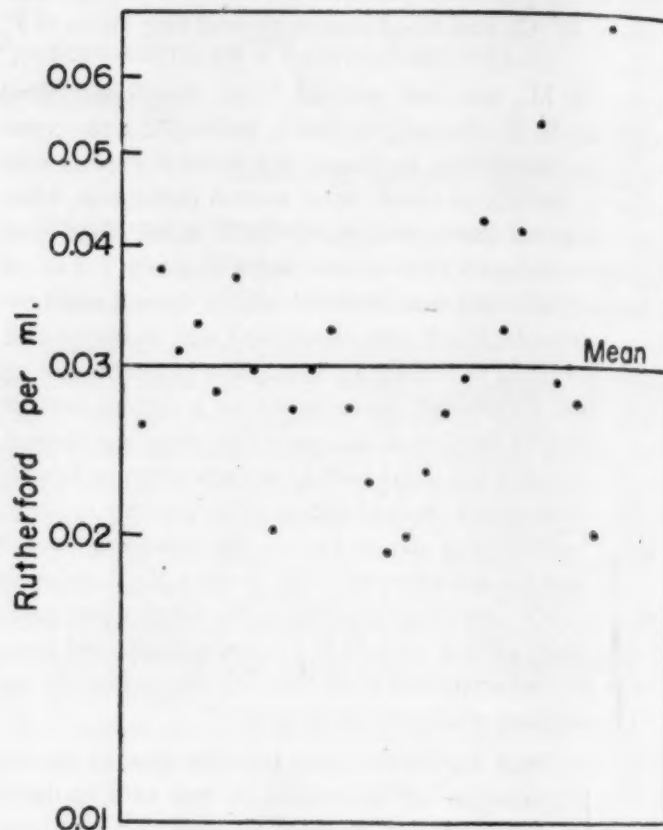


FIG. 1

This preliminary distribution serves only to focus attention on the magnitude of the discrepancies and the need for more accurate standardization. It is certain that much of the variation reported above, in those cases where beta-ray counters were used for measurement, can be reduced by the use of the RaD + E beta-ray standards now available from the National Bureau of Standards. These standards are undoubtedly correct in absolute value to  $\pm 5$  per cent. By the use of the nominal value, as stated in the certificate accompanying these standards, all counter measurements can be placed on a common basis of comparison to a somewhat higher accuracy.

One sample sent out by us was reported contaminated by a growth of streptococcus on receipt by the cooperating institution. The difficulty of bacterial growth in preparation of  $P^{32}$  and  $I^{131}$  has been encountered by others. This indicates that all containers should be carefully sterilized before filling, a precaution which we will adopt in the future. Bacterial contamination interferes seriously in measurements which require preparation of aliquots of the original sample.

Since another program of intercomparison is to be started in the immediate future, we would like to hear from other institutions or investigators who may not have been included in the preliminary distribution and who wish to cooperate in the measurement. The method of distribution of calibrated samples is about the most satisfactory way of standardizing in various laboratories measurements for radioisotopes of half-value period too short for the preparation of permanent standards. The National Bureau of Standards proposes to extend this service to other short-period isotopes as the demand arises.



# Book Reviews

**Thermodynamics for chemists.** Samuel Glasstone. New York: D. Van Nostrand, 1947. Pp. viii + 522. \$8.00. Series price, Vol. I, \$7.00.

This book on elementary chemical thermodynamics should find a receptive audience among students of chemistry and chemical engineers. In a clear, relaxed style the author presents those parts of thermodynamics and statistical mechanics that have stood the test of experiment and may deserve the name canonical. Almost every principle or formula is followed by numerous, well-selected tables, graphs, and problems, and the author has had the grace to work out, numerically, representative examples, so that the reader is not left in doubt as to the units involved. This is in wholesome contrast to the current practice of the proud Shakuntas, who delight in introducing systems of units that confound both the catechumen and the learned.

In the main, the subject matter covered does not extend beyond that given by Gibbs, Lewis and Randall, Fowler, Epstein, and Tolman; but the beginner or the practicing engineer still finds these greater treatises somewhat difficult; and, moreover, he is not yet certain which parts have proved most useful. The author has chosen those having maximum utility.

One may find here, as in all books, debatable statements. For example, the definition of energy (p. 6) causes a pang; the discussion of the exceptions to the so-called third law (p. 196) provokes the reader to wonder whether the third law is true and the crystals imperfect, or the crystals perfect and the third law false.

It is noteworthy that some part of the book was done at the university of a state (Oklahoma) famous for its fertility, fine spirit, and amazing human color. It is characteristic of this country that this same state should give encouragement to a scholar.

When the elite of science, the engineers, and students come to examine *Thermodynamics for chemists*, the first may scoff, but the two latter will probably remain to pray.

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**College technical physics.** Robert L. Weber, Marsh W. White, and Kenneth V. Manning. New York-London: McGraw-Hill, 1947. Pp. viii + 761 (Illustrated.) \$4.50.

This is a general textbook of physics for college students of science and engineering. The order of presentation and treatment of subject matter are conventional and the style straightforward and clear. The use of mathematics is confined to algebra and trigonometry, and even the latter is used sparingly. Calculus is avoided, although the increment notation is occasionally employed.

Numerous solved problems are interpolated at strategic places in the text, and the proper handling of units is carefully

explained. Suggestive questions accompany the problems at the end of each chapter.

The book is well illustrated by numerous line drawings. An interesting feature is the introduction of portrait sketches of the Nobel Prize winners in physics from Röntgen to Bridgman. These are placed in the chronological order of award as chapter headpieces. Though this has an obvious advantage, it also possesses the drawback of providing little or no connection in general between the field of work of the prizewinner and the material of the chapter at the beginning of which his portrait appears. It must be confessed that the poor quality of the paper scarcely does justice to the sketches.

The book is weak on modern physics. Only 16 pages are devoted to 20th-century developments. The quantum theory is disposed of in a few sentences which give no conception of its importance, and relativity is barely mentioned in connection with  $E = mc^2$ . Even such things as the photoelectric effect and thermionic emission get scarcely more than a passing mention. This seems regrettable in a book intended for a fundamental course in elementary physics. For students going on to engineering, the treatment of thermodynamics is not sufficient, and the statement of the second law is not precise. The reviewer regrets to see no definition of mass. It has been shown that this fundamental concept *can* be made clear in an elementary book, and it seems only fair that the student should get it straight, even in his first course.

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**Sequential analysis.** Abraham Wald. New York: John Wiley; London: Chapman & Hall, 1947. Pp. xii + 212. \$4.00.

In the reviewer's opinion this book is very useful and valuable and should be possessed and digested by every teacher of statistics and by every professional statistician.

Sequential analysis, a method of testing statistical hypotheses, consists of making a certain calculation after each observation is made and deciding, on the basis of this calculation, whether to (1) accept the hypothesis under test, (2) accept the alternate hypothesis, or (3) postpone judgment, pending the examination of more data.

The advantages of the method appear to be that (1) it results, on the average, in a great reduction in the number of observations required for a given degree of reliability; (2) it appears simpler than prevailing methods of analysis; and (3) most numerical calculations can be made in advance of collecting the data.

Sequential analysis is a method by which statistical data are analyzed continuously as they become available. In the book there is presented a particular method of sequential analysis, the so-called sequential probability test, to test statistical hypotheses. The idea of sequential analysis is not new. It appears that the idea was first conceived by Romig and Dodge, who gave us a double sampling procedure. Later there was a

multiple-sampling scheme by Bartky, and, also, the idea of chain experiments was discussed by Hotelling in 1941.

In the reviewer's opinion, sequential analysis is not the last word in testing procedures for the general problem of efficient testing. Too little attention appears to be given to operational testing situations to determine the pertinent factors that are involved. However, the technique appears to be useful when the test is destructive and when the cost of testing an item is large.

The book is divided into three parts and an appendix. Part I includes: (1) an elegant discussion of the elements of the current theory of testing hypotheses, (2) a clear and concise general statement of a sequential test of a statistical hypothesis, (3) the nature and meaning of a probability ratio test, and (4) an outline of a theory of sequential tests of simple and composite hypotheses against a set of alternatives. In Part II we have certain simple applications of the theory to very special cases involving the binomial and normal distribution functions. It would have been interesting and useful to have had, in addition, illustrations of less common cases. Part III outlines a possible approach to the problem of sequential multi-valued decisions and estimation. As is well known to the author of the book, this field is unexplored, and in it there is much left to be done. In the appendix the author gives certain mathematical derivations pertinent to the theory of sequential testing.

In the reviewer's opinion, the book is well and clearly written and may be read and understood by those who have no advanced mathematical training.

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**Diseases of the nose and throat.** (3rd ed.) Charles J. Imperatori and Herman J. Burman. Philadelphia: J. B. Lippincott, 1947. Pp. xxvi + 576. (Illustrated.) \$12.00.

This revised standard work is addressed to surgeons and therapists in the field of rhinolaryngology. It stresses the point of view that modern surgery is performed not merely to correct pathology or deformity, but to achieve an optimum postoperative functional result for the patient. The new material introduced in the present edition has to do chiefly with the oral manifestations of nutritional disturbances, vitamin deficiency, and the use of sulfonamides and penicillin, particularly in relation to intracranial complications. The chapter on radiation therapy has been completely revised in the light of recent clinical research. The volume is presented as a working manual for the diseases of the nose and throat written in terse sentences and arranged in well-outlined, almost tabular, form. The condensed text is complemented by 480 good illustrations, a large number of them actual photographs and a fair number in color. Supplementing 49 chapters by the authors are three by other contributors: Frederick M. Law, on "Roentgen Examination of Nasal Accessory Sinuses"; Ira I. Kaplan, on "Radium and Roentgen Ray"; and Andrew A. Eggston, on "Laboratory Aids." Although the volume is supplied with a very good index, it is almost wholly lacking in references to pertinent literature and leaves the reader at a complete loss in reference to the sources for statements made or where further elaboration of techniques and topics could be secured.

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## Scientific Book Register

BOURIQUET, G. *Les maladies des plantes cultivées à Madagascar*. Paris: Paul Lechevalier, 1946. Pp. 545. (Illustrated.) 1200 fr.

BOYCE, JOSEPH C. (Ed.) *New weapons for air warfare*. (Science in World War II, OSRD.) Boston: Little, Brown, 1947. Pp. xviii + 292. (Illustrated.) \$4.00.

CAHALANE, VICTOR H. *Mammals of North America*. New York: Macmillan, 1947. Pp. x + 682. (Illustrated.) \$7.50.

CARSWELL, T. S. *Phenoplasts: their structure, properties, and chemical technology*. New York-London: Interscience, 1947. Pp. xii + 265. \$5.50.

CROWTHER, J. A. (Ed.) *Handbook of industrial radiology*. (Industrial Radiology Group, Institute of Physics.) London: Edward Arnold, 1946. Pp. viii + 203. (Illustrated.) \$7.00.

DEGERING, ED. F., and collaborators. *The work book of fundamental organic chemistry*. Ypsilanti, Mich.: Univ. Lithoprinters, 1947. (Rev. ed.) Pp. 256. (Illustrated.) \$1.75.

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EASTMAN, E. D., and ROLLEFSON, G. K. *Physical chemistry*. New York-London: McGraw-Hill, 1947. Pp. viii + 504. \$4.50.

HALDANE, J. B. S. *Science advances*. New York: Macmillan, 1947. Pp. 253. \$3.00.

KRAEHNBUHL, JOHN O., and FAUCETT, MAX A. *Circuits and machines in electrical engineering*. Vol. I: *Circuits*; Vol. II: *Machines*. (2nd ed.) New York: John Wiley; London: Chapman & Hall, 1947. Pp. ix + 367; ix + 370. (Illustrated.) \$4.25 ea.

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NELSON, J. RALEIGH. *Writing the technical report*. (2nd ed.) New York-London: McGraw-Hill, 1947. Pp. xiv + 388. \$3.00.

NORD, F. F. (Ed.) *Advances in enzymology and related subjects of biochemistry*. (Vol. VII.) New York-London: Interscience, 1947. Pp. xi + 665. \$8.75.

—. *Heredity and variation in microorganisms*. (Cold Spr. Harb. Sympos. quant. Biol., Vol. XI.) Cold Spring Harbor, N. Y.: Biological Laboratory, 1946. Pp. xi + 314. (Illustrated.) \$6.00.